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Prevalence and Predictors of Abnormal Cervical Cytology in HIV-Infected Patients at the Anonymous Clinic, Chonburi Hospital

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ABSTRACT

Objective: To categorize prevalence and predictors of abnormal cervical cytology among HIV-infected women at the anonymous clinic, Chonburi hospital.

Method: We screened 280 non-pregnant HIV-infected women accessing HIV/AIDS care service at the anonymous clinic, Chonburi hospital. We collected cervical specimens for cytological analysis by conventional Papanicolaou smear (Pap smear). Multivariate logistic regression analysis was employed and calculated based on following factors: sociodemographic, CD4 + cell counts, medical, sexual variables and gynecologic history.

Results: Prevalence of abnormal cervical cytology from Pap smear in HIV-infected women was 21.3%(60/280), of which 0.7%(2/280) had atypical squamous cells exclude high grade lesion (ASC-H), 6.4%(18/280) had low grade squamous intraepithelial lesion (LSIL), 12.1%(34/280) had high-grade squamous cell intraepithelial lesion (HSIL) and 2.1%(6/280) had squamous cell carcinoma (SCCA). Multivariate logistic regression analysis suggested that number of parity, lifetime sexual partners, age of first intercourse at 18 years or younger and lowest CD4+ cell count were significantly associated with the presence of the abnormal cytological lesions (adjusted OR: 1.515, 95%CI 0.036-2.214, p=0.032, adjusted OR: 2.938, 95%CI 1.874-4.607, p<0.001, adjusted OR: 0.401, 95%CI 0.191-0.842, p=0.016, adjusted OR: 0.993, 95%CI 0.990-0.996 p<0.001, respectively). In addition to these factors, univariate analysis also identified additional factors significantly associated with the presence of abnormal cytological lesions (≥ASC-H). Such factors were duration of HIV-infectio n, current CD4+ cell counts, and antiretroviral drug therapy.

Conclusion: In our population, the independent predictors of abnormal Pap smear in HIV infected women were number of parity, lifetime sexual partners, age of first intercourse at 18 years or younger and lowest CD4+ cell counts.

Keywords: pap smear, HIV infected patient, predictor

Human Immunodeficiency Virus (HIV) infection is a major public health problem faced by almost all nations including Thailand. Recent study showed that cervical HPV infection and SIL were significantly

higher in HIV-positive women compared with risk-matched HIV-negative women.[1] In the United States, HIV-positive women were 4-10 times more susceptible for cervical intraepithelial neoplasia (CIN).[2] The American Center of Disease Control and Prevention (CDC) also suggested that HIV-infected women should receive a complete gynecologic evaluation including a Pap smear test every six months. If two consecutive test results show no evidence of SIL, the subject should have a Pap smear repeated once a year.[3,4] Revised CDC system for HIV-infected patient categorizes person on basis of clinical condition associated with HIV infection and CD4+ cell counts. Moreover, invasive cervical cancer and cervical intraepithelial neoplasia are clinical conditions indicating category 2 and category 3, respectively. However, Pap smear screening in all HIV-infected patients based on CDC recommendation does not consider immune status or any gynecologic data. This paper reports the results of the prevalence of cervical cytologic abnormalities in these women and its relation to their immunosuppressive state including gynecologic and socioeconomic data.

Materials and Methods

This present research was designed as a prospective descriptive study. The study was approved by the Chonburi hospital ethics committee. We recruited 280 non-pregnant HIV-infected women attending the anonymous clinic at Chonburi Hospital from June 1, 2007 to May 28, 2008. After the explanation of the study and clinical procedures, each of all 280 subjects were provided written consent administered in Thai. Eligibility criteria included prior documented evidence of HIV infection (2 positive ELISA) and good mental and physical conditions. We excluded women who were pregnant, had a previous diagnosis and treatment of cervical dysplasia or cervical carcinoma, or had undergone hysterectomy, Loop Electrosurgical Excision Procedure or cervical conization.

Basic sociodemographic and gynecologic data were collected using a structured questionnaire. The outpatient department(OPD) cards were reviewed and lowest CD4+ cell counts and current CD4+ cell counts data were collected. A trained gynecologist conducted pelvic examination and collected specimens for Pap smears from posterior fornix, ectocervix and endocervix (VCE technique) using a wooden Arye spatula. Specimen with single slide in Pap smear technique was immediately fixed with 95% alcohol. All the Pap smear tests were classified based on the Bethesda system (2001) and interpreted by a cytotechnologist, who had no knowledge of whether the specimen belonged to an HIV-infected patient or an HIV-negative patient. In addition, all abnormal Pap smears were interpreted by a medical cytologist. Data were collected and analyzed for the prevalence of abnormal cervical cytology in HIV-infected women. These factors were analyzed using univariate and multivariate logistic regression tests as appropriately. P-value of <0.05 was considered to be statistically significant.

Results

Sixty subjects in our study had abnormal cervical cytology from ASC-H to SCCA level and the other 220 subjects had normal cervical cytology. We included 2 subjects with ASC-H level into HSIL group because the baseline data suggested that the incidences of CIN II, III from biopsy in this group were high (41%).[7] Demographical characteristics and gynecologic history of patients in this present study are shown in Table 1. Table 2 represents prevalence of abnormal cervical cytology in HIV-infected women was 21.3%(60/280), of which 0.7%(2/280) had atypical squamous cells can not exclude high grade lesion (ASC-H), 6.4%(18/280) had low grade squamous intraepithelial lesion (LSIL), 12.1%(34/280) had high-grade squamous cell intraepithelial lesion (HSIL) and 2.1%(6/280) had squamous cell carcinoma (SCCA). The univariate logistic regression analysis indicated statistical significant association between parity, age of first sexual intercourse at 18 years or younger, lowest CD4+ cell counts, current CD4+ cell counts and the history of antiretroviral therapy (Table 3). The

multivariate logistic regression analysis indicated statistical significance association between number of parity, number of lifetime sexual partners, age of first intercourse at 18 years or younger and lowest CD4+ cell counts (Table 3).

The abnormal Pap smear group, 60 patients, was further investigated to prove histopathology by colposcope with biopsy. 11 cytologic results had more severe compared with histopathology, 5 cytologic results had less severe, 40 person had confirmed lesion correctly and 4 persons loss to follow up.

Table 1. Demographic characteristic of HIV infected patients

Characteristics	N (280)
Age (years)	
≤35	124 (44.3%)
>35	146 (55.7%)
Income (baht)	
≤5000	85 (30.4%)
5001-10000	136 (48.6%)
10001-30000	57 (20.4%)
≥30001	2 (0.7%)
Smoking	
No smoking	270 (96.4%)
Smoking	10 (3.6%)
Duration (years)	
≤10	245 (87.5%)
>10	35 (12.5%)
Lowest CD4+ count (X106/L)	
<200	147 (52.5%)
200-500	119 (42.5%)
>500	14 (5.0%)
Current CD4+ count(X106/L)	
<200	28 (10.0%)
200-500	166 (59.3%)
>500	86 (30.7%)
Antiretroviral therapy(HAART)	
No	50 (17.9%)
Yes	230 (82.1%)
Parity	
≤1	170 (63.2%)
>1	110 (36.8%)
Age of 1st sexual intercourse (years-old)	
≤18	91 (29.1%)
>18	189 (70.9%)
Number of sexual partners	
1	88 (35.9%)
>1	192 (64.1%)

Table 2. Frequency of cervical cytology results among HIV-infected women

Pap smear	Frequency (N=280)
Normal	115 (41.1%)
Benign cellular change	98 (35.0%)
ASC-US	7 (2.5%)
ASC-H	2 (0.7%)
LSIL	18 (6.4%)
HSIL	34 (12.1%)
SCCA	6 (2.1%)

Table 3. Univariate and multivariate logistic regression analysis for the predictors of SIL and SCCA

Variable	Univariate analysis OR [95% CI]	p value	Multivariate analysis Adjusted OR [95% CI]	p value
Age	0.997	0.861 [0.962-1.033]	0.966	0.183 [0.918-1.016]
Income	0.724	0.100 [0.492-1.064]	0.992	0.973 [0.614-1.602]
Smoking	0.914	0.911 [0.189-4.421]	0.795	0.794 [0.143-4.438]
Parity	1.444	0.022 [1.053-1.981]	1.515	0.032 [1.036-2.214]
Lifetime sexual partner	3.033	<0.001 [2.042-4.504]	2.938	<0.001 [1.874-4.607]
Age at 1st SI				
≤18 yrs	0.501	0.021 [0.279-0.901]	0.401	0.016 [0.191-0.842]
> 18 yrs	1		1	
Duration	1.111	0.011 [1.024-1.205]	1.088	0.148 [0.971-1.218]
Lowest CD4+ counts	0.994	<0.001 [0.996-1.000]	0.993	<0.001 [0.990-0.996]
Antiretroviral drugs	2.829	0.036 [1.070-7.479]	1.214	0.732 [0.401-3.678]
Current CD4+ counts	0.998	0.012 [0.996-1.000]	-	-

Discussion

HIV infection is a major public health problem in Thailand and worldwide. From 1984 to 2007, there were 330,740 Thai's with HIV-infection and the total death caused by HIV was 91,8396. Cervical dysplasia and invasive squamous cell CA were symptomatic HIV infection.3 387 Thai HIV-infected women suffer from invasive cervical cancer since 1984.[6] In addition, compared with their HIV-negative, HIV-positive women have a greater incidence of both cervical intraepithelial neoplasia and invasive cervical cancer thus these lesions are also more progressive and aggressive.[7,8]

Our present study aimed to search for the predictors of abnormal cervical cytology in HIV-infected patients in Chonburi hospital. The deviation from past studies was that we grouped ASC-H data into the abnormal Pap smear group due to the high incidence of high grade cervical dysplasia (41%) 5 compared to ASC-US where the incidence is quite low (4-12%).[9,10] The prevalence of abnormal Pap smears at 21.3% in this study is consistent with results from previous studies which showed the prevalence in HIV-infected women ranged from 14 to 30%.[11]

Level of immune status of HIV-infected patient evaluated by current CD4+ cell counts related to the

occurrence of SIL in past studies.[1,12,13] Our results suggested lowest CD4+ cell counts documented in OPD card was one of the independent factor of abnormal Pap smear (p value<0.001) whereas multivariate logistic regression shows that current CD4+ cell counts was not an independent risk factor. It is possible that high level of current CD4+ cell count from immune restituition after antiretroviral treatment did not represent the worst immunosuppression status. We implied that the abnormal cervical cytology may be related to the worst immune status represented by lowest CD4+ cell counts.

The 9,769 Pap smear specimens collected from gynecologic OPD case at the same period of our study were transferred to the Pathology department, Chonburi hospital for interpretation. The prevalence of abnormal Pap smear in this population was 3.1% which was 7 times less than HIV-infected patient. These results indicate the crucial importance of screening HIV-infected women especially in case that they represent important independent predictors such as low CD4+ cell counts, historical evidence of more severe immunosuppression condition, young age at the 1st sexual intercourse, high number of parity, or high number of lifetime sexual partners. We also consider whether this present recommendation be an adequate screening in all condition of HIV infected patients. In the case where patients show these factors implicating more potential to be CIN or SCCA, the necessity to early diagnosis and more sensitive Pap smear screening method or HPV DNA testing may be more appropriated. The availability of cost-effectiveness screening and benefit will need additional studies.

Furthermore, our study has important limitations. First, presence of high-risk HPV was the important independent predictor of CIN and SCCA. [14,15] We could not include HPV DNA testing in our study due to funding restriction. HIV-infected patients who were recruited into our study cannot be systemic randomized because of the patient rejection to give consent after the explanation of the study and clinical procedure.

According to our results, the number of parity, number of lifetime sexual partners, age of first intercourse at 18 years or younger and lowest CD4+ cell counts were the independent predictors of abnormal Pap smear and therefore it is advisable to perform frequent cervical screening or high sensitive, less false negative Pap smear screening methods in patient who have such factors and the availability of cost-effectiveness screening and benefit will need additional studies.

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ความชุกและปัจจัยทำนายของการเกิดความผิดปกติของเซลล์เยื่อบุผิวปากมดลูก ในสตรีผู้ติดเชื้อเอชไอวี ที่คลินิกนิรนาม โรงพยาบาลชลบุรี

พิมพิกา ตันสุภสวัสดิกุล, สมคิด ปิยะมาน

วัตถุประสงค์ *: เพื่อศึกษา ความชุกและปัจจัยทำนายการเกิดความผิดปกติของเซลล์เยื่อบุผิวปากมดลูก ในผู้ป่วยติดเชื้อเอชไอวี ที่คลินิกนิรนาม โรงพยาบาลชลบุรี*

วัสดุและวิธีการ *: สตรีผู้ติดเชื้อเอชไอวี มารับการรักษาที่คลินิกนิรนาม โรงพยาบาลชลบุรี 280 คน ตั้งแต่ 1 มิถุนายน 2550-30 พฤษภาคม 2551 สตรีที่เข้าร่วมการศึกษาได้รับการตรวจคัดกรองมะเร็งปากมดลูก ด้วยวิธี conventional Papanicolaou smear (VCE technique) และได้เก็บข้อมูลพื้นฐานทางสังคม ประวัติทางสูตินรีเวชกรรม ประวัติการรักษา จำนวนเม็ดเลือดขาว CD4+ ที่ต่ำที่สุดตั้งแต่เริ่มต้นการรักษา และ ระดับ CD4+ ในปัจจุบัน ปัจจัยดังกล่าวนำมาวิเคราะห์ทางสถิติ เพื่อศึกษาปัจจัยทำนายการเกิดความผิดปกติของเซลล์เยื่อบุผิวปากมดลูก และความชุกของการเกิดความผิดปกติของเซลล์เยื่อบุผิวปากมดลูก*

ผลการศึกษา *: สตรีที่ติดเชื้อเอชไอวีมีความชุกของการเกิดความผิดปกติของเซลล์เยื่อบุผิวปากมดลูก ร้อยละ 21.3 (60/280) ได้แก่ กลุ่ม atypical squamous cells can not exclude high grade lesion (ASC-H) คิดเป็นร้อยละ 0.7 (2/280), low grade squamous intraepithelial lesion (LSIL) คิดเป็นร้อยละ 6.4 (18/280), high-grade squamous cell intraepithelial lesion (HSIL) คิดเป็นร้อยละ 12.1 (34/280) และ squamous cell carcinoma (SCCA) คิดเป็นร้อยละ 2.1 (6/280). เมื่อนำมาวิเคราะห์ด้วย multivariate logistic regression พบว่าจำนวนการคลอดบุตร จำนวนคู่นอน อายุเมื่อเริ่มมีเพศสัมพันธ์น้อยกว่าหรือเท่ากับ 18 ปี และระดับ CD4+ ที่ต่ำที่สุดตั้งแต่เริ่มการรักษา มีความสัมพันธ์กับการเกิดความผิดปกติของเซลล์เยื่อบุผิวปากมดลูกอย่างมีนัยสำคัญ(adjusted OR: 1.515, 95% p=0.032, adjusted OR: 2.938, 95%CI, p<0.001, adjusted OR: 0.401, 95%CI, p=0.016, adjusted OR: 0.993, 95%CI p<0.001 ตามลำดับ)*

สรุป *: ปัจจัยอิสระของการเกิดความผิดปกติของเซลล์เยื่อบุผิวปากมดลูกในหญิงที่ติดเชื้อเอชไอวี ได้แก่ จำนวนการคลอด จำนวนคู่นอน อายุเมื่อเริ่มมีเพศสัมพันธ์น้อยกว่าหรือเท่ากับ 18 ปี และระดับ CD4+ ที่น้อยที่สุดตั้งแต่ได้รับการรักษา*