Associated Risk Factors of Human Papillomavirus Cervical Infection Among Human Immunodificiency Virus-Seropositive Women at Siriraj Hospital

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Abstract

This cross sectional type sub-study was established to assess the potential risk factor associated with human papillomavirus (HPV) cervical infection in Human immunodeficiency virus (HIV)-seropositive women.

The series of 178 HIV-seropositive women was enrolled in the Department of Obstetrics & Gynecology, Siriraj Hospital. Demographic, obstetrical and behavioral risk factors were interviewed. Laboratory results were recorded. Clinical gynecologic examination was performed including Pap smear. The patients were assigned into two groups, HPV and non-HPV group. The comparison of the potential risk factors between the groups was calculated statistically.

It was found that the prevalence of HPV infection was reported in 17 patients (9.6%). HIV-seropositive women, who were infected with HPV, had a significantly more probability to have a single partner in their lifetime than those who were not infected.

It could be that HPV cervical infection and HIV-seropositive women share common potential risk factors, as well as, the recognition of sexual intercourse as the important route of HPV transmission.

Key word : Human Papillomavirus, Risk Factor, Human Immunodeficiency Virus

SIRIMAI K, CHALERMCHOCKCHAROENKIT A, ROONGPISUTHIPONG A, PONGPRASOBCHAI S
J Med Assoc Thai 2004; 87: 270-276

The issue about human papillomavirus (HPV) has become an interesting topic from many different points of views. Such as discovering a new subtype of HPV, a new method to attack HPV, the linking between specific HPV type with any different clinical lesion, as well as the correlation between human

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papillomavirus cervical infection and cervical neoplasia, which has been reported consistently[1,2].

Nevertheless, HPV infection of the lower genital tract, including the cervix, has become more prevalence worldwide, especially in those who were infected with human immunodeficiency virus (HIV), however the relationship between HPV and HIV remains in the study. Because HPV and HIV are both viral sexually transmitted diseases, they may share nearly the same risk factors.

However, a study about associated risk factors for HPV infection, especially in Thai women has not been well documented. This may be due to the difference in the study populations and the viral detection method used.

The aim of this study was to assess the potential risk factors associated with human papillomavirus cervical infection, especially in HIV-seropositive women, using data from the Division of Gynecologic Infection and Sexually Transmitted Disease, Siriraj Hospital.

MATERIAL AND METHOD

A cross sectional type sub-study was established following the main project concerning the usefulness of Zidovudine for the prevention of mother to child HIV-transmission. The main project was conducted by the HIV/AIDS Collaboration (HAC), a joint activity of the Thailand Ministry of Public Health and the US Center for Disease Control and Prevention, during the years 1996 and 1997.

178 women, who were documented with HIV-infection without AIDS condition as defined by the US Centers for Disease Control and Prevention in 1987, were recruited from the patients who attended the Female Sexually Transmitted Disease Clinic, Siriraj Hospital, in Bangkok.

All eligible women were given information about the study after post test counseling. The participants then had to sign a written consent form. All participants underwent a detailed interview dealing with their medical, social and drug use history, which also included the history of their partners. HIV and HPV infection, demographic, obstetric and behavioral risk factors were also determined.

All participants underwent a standard gynecologic examination, during which smears (Papanicolaou stain) were obtained from the endocervix, cervical transformation zone and vagina, described as a VCE technique for cytological analysis. The cytological report contained the description and HPV infection was also diagnosed by this technique.

Laboratory results such as viral load and CD 4 counts were done in a local laboratory conducted by HAC.

Characteristics of all participants were described using means, standard deviation (SD), and percentage. Comparison between groups was calculated statistically by Student's *t*-test and Chi-square test as appropriate. (SPSS 10.0 for Windows and Epi Info Version 6, Centers for Disease Control and Prevention (CDC), Atlanta, Ga). Logistic regression was used in determining independent risk factors, adjusting for potential confounders. P-value < 0.05 was considered statistically significant.

RESULTS

At the end of the study, 178 HIV-seropositive women were enrolled at Siriraj Hospital. However, from the cytological analysis, the authors only found 17 patients (9.6%) who were infected with HPV.

Characteristics of the 17 HIV-seropositive women, who had an abnormal Pap smear for HPV infection, and also with their partners' characteristics, are shown in Table 1. There was no difference between both groups, HPV and non-HPV, statistically.

Concerning the potential risk factors, Table 2 demonstrates the patient's risk factors associated with HPV infection. Table 3 also shows the relative risk factors associated with the spouse of the patients.

For all risk factors, there was a trend of the HIV-seropositive patients who were infected with HPV to have the first pregnancy between the age of 21 to 25 years old. It was also found that HPV infected women had more probability to have single partners than the patients who were infected with HIV alone, significantly (p-value < 0.05).

DISCUSSION

Human papilloma virus (HPV) is the one that belongs to the Family Papovaviridae. In the past decade, Papanicolaou stain for cytological analysis was promoted in Thailand for cervical cancer screening. The one, that took response for the abnormal findings, is HPV. There is more concern with this viral infection of the female lower genital tract, because it is associated with more prevalence of cervical cancer[1,3]. Even the issue about HPV became popular world-

wide, but in Thailand, only a few studies have been published[1,3].

In fact, the general prevalence of sexually transmitted disease has decreased. However, the trend of viral infection, such as human immunodeficiency virus (HIV) and human papilloma virus (HPV), has been the opposite. This finding also corresponds with the report in 1998 by Siriwasin, et al[4]. They stated that there was more increase in new HIV-seropositive cases, especially in Asia and in women of reproductive age.

Because of the responsibility of our clinic to take care of HIV-seropositive women who attend the outpatient clinic of the Department of Obstetrics and Gynecology, Siriraj Hospital, the authors found the prevalence of HPV cervical infection among HIV-seropositive women around 9.6 per cent. The prevalence may be lower than other reports because the authors use the Pap smear as a standard method for cervicovaginal screening, even for HIV-seropositive women. The sensitivity of this screening technique may be low when compared to others such as, HPV-DNA detection by polymerase chain reaction (PCR) [1,5,6]. However, prevalence rates of 3-50 per cent were reported in various populations[1].

In order to reduce the prevalence of HPV cervical infection, it is important to know the patients who are at most risk. The authors established this study to find out the potential risk factors that prominent from the patients at risk, HIV-seropositive patients. Not only the patients but also the risk factors of their partners should be investigated because the HIV transmission to these non-female sex workers in Thailand is presumed that most comes from their husbands or their partners. Several studies have also commented about the potential risk factors for these groups of women at risk because of the risk behaviors of their partners, too[4,7].

HIV infection is also one of the important risk factors for HPV cervical infection. Many studies have shown the higher rate of HIV infection among women who had HPV related diseases and vice versa [8-10]. The prevalence of HPV lesions in persons with acquired immunodeficiency syndrome (AIDS) has also been reported to increase with immunosuppression, but it is unclear whether this reflects a permissive effect related to impaired immune function or a direct interaction of the viruses[11].

Because the main form of HPV transmission is sexual intercourse, so sexual behavior has become the most important determinant of genital HPV infection[12,13]. Initiation of sexual intercourse at an early age, multiple sex partners, and sex partners who have multiple sex partners are significant risk factors[7, 12,14,15]. Kataya et al demonstrated the strongest independent risk factor, the number of sexual partners during the previous 2 years[12].

From Table 1, shows the general characteristics of the patients who had abnormal Pap smears for HPV. The characteristics were nearly the same between HIV-seropositive women who carried HPV and those who did not.

Concerning the risk factors of the special group, Hankins reported the risk factors associated with HPV in women living with HIV such as; low CD4 count, non-white race, inconsistent condom use and lower age[16], which could not be demonstrated from the present study. There is more probability for HIV-seropositive women who are infected with HPV to have the first pregnancy between the ages of 21 to 25 years old as well as having only a single partner in their life. From this finding, it means that HPV genital

Table 1. Demographic data.

Characteristic	HPV group (n = 17) (mean ± SD)	Non HPV group (n = 161) (mean ± SD)	P-value*
Age (years)	23.9 ± 3.9	24.7 ± 4.7	0.49
Age at first pregnancy (years)	21.6 ± 2.7	21.9 ± 4.0	0.83
Age at first intercourse (years)	19.4 ± 2.6	19.5 ± 3.7	0.96
Family income (Baht/month)	13,447.1 ± 14,744.2	11,953.4 ± 14,405.9	0.69
CD4 Lymphocyte (cell/mm^3)	441.9 ± 182.9	441.5 ± 206.6	0.99
Log viral load	4.6 ± 0.6	4.4 ± 0.7	0.26
Partner's age (years)	29.0 ± 7.3	29.0 ± 6.4	0.98

* Student's *t*-test

Table 2. Risk factors assessed for potential association with HPV infection.

Characteristic	HPV group (n = 17)	%	Non HPV group (n = 161)	%	Odd ratio	P-value*
Age (years)					1.21 (0.39-3.90)	0.72
Younger age (Equal or < 25 years)	11	64	97	60.2		
> 25 years	6	35.3	64	39.8		
Age at first pregnancy (years)					2.85 (0.92-9.19)	0.04**
Age between 21-25 years	11	64.7	63	39.1		
Others	6	35.3	98	60.9		
Age at first intercourse (years)					0.76 (0.25-2.31)	0.59
Teenager (< 20 years)	9	52.9	96	59.6		
Equal or > 20 years	8	47.1	65	40.4		
Education					1.67 (0.51-5.73)	0.35
Primary school or lower	12	70.6	95	59		
Higher than primary school	5	29.4	66	41		
Career					0.75 (0.19-2.64)	0.62
Skilled	4	23.5	47	29.2		
Nonskilled	13	76.5	114	70.8		
Migration in the past year					2.09 (0.68-6.37)	0.15
Yes	8	47.1	48	29.8		
No	9	52.8	113	70.2		
Regularity of partnership					1.06 (0.12-23.5)	0.95
Yes	16	93.7	151	93.8		
No	1	6.3	10	6.2		
Socioeconomic status					1.21 (0.39-3.90)	0.72
Upper/middle	11	64.7	97	60.6		
Low income (< 10,000 baht/month)	6	35.3	64	39.4		
Lifetime number of different sex partners					3.54 (1.09-12.19)	0.02**
1	12	70.6	65	40.4		
2 or more	5	29.4	96	59.6		
Commercial sex worker					2.01 (0-11.33)	0.38
Yes	2	11.8	10	6.2		
No	15	88.2	151	93.8		
History of STD infection					0.94 (0.2-3.8)	0.92
Yes	3	17.6	30	18.6		
No	14	82.4	131	81.4		
History of Gonorrheal infection					0.66 (0.03-5.36)	0.69
Yes	1	5.9	14	8.7		
No	16	94.1	147	91.3		
VDRL seropositive					1.61 (0.2-12.35)	0.66
Yes	1	5.9	6	3.7		
No	16	94.1	155	96.3		
CD 4 count					0.64 (0.21-2.01)	0.39
Equal or < 500	10	58.8	111	68.9		
> 500	7	41.2	50	31.1		
Log viral load					0	0.46
Equal or < 3	0	0	5	3.1		
> 3	17	100	156	96.9		
History of partner being bisexual (n = 174)					1.57 (0.23-9.71)	0.68
Yes	1	5.9	6	3.8		
No	16	94.1	151	96.2		

* Chi-square test

** Statistical significance at p-value less than 0.05

Table 3. Associated partner's risk factors for HPV infection.

Characteristic	HPV group (n = 16)	%	Non HPV group (n = 151)	%	Odd ratio	p-value*
Age (years)					0.69 (0.18-2.49)	0.54
Younger age (Equal or < 25 years)	4	25	49	32.5		
> 25 years	12	75	102	67.5		
Education					0.44 (0.11-1.57)	0.16
Primary school or lower	4	25	65	43		
Higher than primary school	12	75	86	57		
Career					1.05 (0.32-3.36)	0.93
Skilled	6	37.5	55	36.4		
Nonskilled	10	62.5	96	63.6		
HIV status (n = 129)					1.00 (0.29-3.65)	1.00
HIV-seropositive	10	66.7	76	66.7		
HIV-seronegative	5	33.3	38	33.3		

* Chi-square test

infection is a disease of the active reproductive age. The authors also demonstrated the importance of the male partner and sexual intercourse as the main transmission route. Having only one sexual partner in the patient's life, who had more risk for HPV infection, can be transmitted to a patient the HPV. In fact, the HPV infected women may receive the disease from other routes, but many aspects of HPV transmission are still unknown and under discussion. The present result confirmed that these HPV infected women are also at risk because of the risk behavior of their partners[4,7]. Hagensee, et al also agreed with the role of sexual activity as the main route of HPV transmission[17].

The authors conclude that both HIV and HPV infections share nearly the same common potential risk factors and the recognition of sexual intercourse as the important route of HPV transmission.

This study aimed to initiate guidelines for the systematic care of women who are infected with HPV, especially in HIV-seropositive women. Because the infection of HPV is the beginning point, many problems will follow. However, more studies about HPV are needed in the future.

(Received for publication on October 27, 2003)

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การศึกษาปัจจัยเสี่ยงต่อการติดเชื้อไวรัส Human papilloma ที่ปากมดลูกในผู้ติดเชื้อเอ็ชไอวี โรงพยาบาลศิริราช

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การวิจัยเชิงวิเคราะห์แบบตัดขวางนี้ เพื่อศึกษาถึงปัจจัยเสี่ยงต่อการติดเชื้อไวรัส Human papilloma ที่ปากมดลูกในสตรีผู้ติดเชื้อเอ็ชไอวี

สตรีผู้ติดเชื้อเอ็ชไอวี จำนวน 178 ราย ได้เข้ามารับการรักษาในภาควิชาสูติศาสตร์-นรีเวชวิทยา โรงพยาบาลศิริราช ผู้ป่วยจะได้รับการตรวจภายในและตรวจหามะเร็งปากมดลูกด้วยวิธี Pap smear ข้อมูลของผู้ป่วยเป็นข้อมูลที่ได้จากการสัมภาษณ์ร่วมกับผลการส่งตรวจทางห้องปฏิบัติการ สตรีผู้ติดเชื้อเอ็ชไอวี จะถูกแบ่งเป็น 2 กลุ่ม คือกลุ่มผู้ป่วยที่ตรวจพบและไม่พบเชื้อไวรัส Human papilloma จากนั้นจึงนำมาวิเคราะห์ทางสถิติ

อุบัติการณ์การตรวจพบการติดเชื้อไวรัส Human papilloma ในสตรีผู้ติดเชื้อเอ็ชไอวี เท่ากับร้อยละ 9.6 ทั้งนี้เมื่อเปรียบเทียบระหว่างทั้ง 2 กลุ่ม พบว่าสตรีผู้ติดเชื้อเอ็ชไอวี ที่ตรวจพบเชื้อไวรัส Human papilloma มีโอกาสที่จะมีคู่นอนเพียงคนเดียวมากกว่ากลุ่มที่ตรวจไม่พบเชื้อไวรัส Human papilloma อย่างมีนัยสำคัญทางสถิติสำหรับปัจจัยอื่น ๆ นั้นไม่พบว่ามีความแตกต่างกัน

สรุปว่า การติดเชื้อไวรัส Human papilloma ที่ปากมดลูกและการติดเชื้อเอดส์ มีปัจจัยเสี่ยงโดยรวมร่วมกันและการมีเพศสัมพันธ์เป็นทางแพร่กระจายเชื้อที่สำคัญ

คำสำคัญ : ไวรัสฮิวแมน ปาปิโลมา, ปัจจัยเสี่ยง, ผู้ติดเชื้อเอดส์

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