RESEARCH ARTICLE

Prevalence and Genotype Distribution of HPV among Women Attending a Cervical Cancer Screening Mobile Unit in Lampang, Thailand

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Abstract

A growing body of literature is evidence that identifying subtypes of high-risk human papillomavirus (HR-HPV) has impacted on various steps of cervical cancer prevention.Thus, it is mandatory to determine the background prevalence and distribution of HPV subtypes for designing and implementing area-specific management. The present study was conducted to evaluate prevalence and distribution of HPV subtypes among women aged 30-70 years living in Lampang, an area with a high incidence of cervical cancer, through use of a mobile screening unit. Of 2,000 women recruited in this study, 108 (5.40%, 95%CI: 4.45-6.48) were found to have HR-HPV infection. Risk was significantly correlated with age and number of partners. Singly or in combination, the most common genotype was HPV 52 (17.6%), followed by HPV 16 (14.81%), HPV 58 (13.89%), HPV 33 (11.11%), HPV 51 (11.11%), and HPV 56 (9.26%). HPV 18 was found in only 5.6% of cases. Together, HPV 16/18 were noted in approximately 20.4% of cases. Eighteen(16.67%) women were positive with multiple subtypes of HR-HPV. Co-infection most frequently involved HPV 16 or HPV 58. These findings have obvious implications for vaccine policy.

Keywords: Cervical cancer screening - human papillomavirus - genotyping - prevalence

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Introduction

Cervical cancer remains the major health problem among Thai women, particularly among those living in Northern Thailand. In the recent population-based survey, areas reported to have a highest incidence of cervical cancer are in Northern Thailand. In Chiang Mai Province, an age-standardized incidence rate (ASR) of cervical cancer is 28.9 per 100,000, followed by Lampang Province (ASR, 22.4) (Moore et al., 2010).

Infection with certain subtypes of human papillomavirus (HPV), the so-called "high-risk (HR)" or "oncogenic type" is a necessary step in cervical carcinogenesis. Growing body of literature show that identifying type-specific HPV infections has impacted on various steps of cervical cancer prevention. For primary prevention,efficacy of prophylactic HPV vaccine, a type-specific vaccine depends on genotype distribution of oncogenic HPV in each population. In screening approach, women with cytology-negative/HR-HPV positive carry a certain risk of harboring high-grade cervical disease which is even more striking among those with HPV 16/18(Khan et al., 2005; Wright et al., 2011). Additionally, subtype of HR-HPV has been note to influence the performances of colposcopy (van der Marel et al., 2014). Findings obtained from a meta-analysis reviewing the worldwide prevalence and genotype distribution of HPV show a substantial geographical variation in the relative frequency of each different HPV subtypes (de Sanjose et al., 2007). Thus, it is mandatory to determine the background prevalence and distribution of HR-HPV subtypes for designing and implementing area-specific management. Accordingly, this study was conducted to evaluate prevalence and distribution of HPV subtypes among women living in Lampang Province, an area with a high incidence of cervical cancer, through mobile screening unit.

Materials and Methods

This study was approved by the institutional review board ofLampang Cancer Hospital. During January 2013 to March 2013, we conducted a mobile unit for cervical cancer screening to enroll the participants aged 30-70 years. Participants proportional to the size of the population of each area across Lampang Province were selected among women who attended our mobile unit. Screening methods includedliquid-based cytology and HR-HPV test (14 HR-HPV types). Participants were interviewed by a trained interviewer using a standardized questionnaire to elicit information on the baseline characteristics variables, sexual behavior, reproductive history and smoking habits. Pregnant women were excluded, as well as women with

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a previous history of abnormal cervical cytology of any grade or cancer of any site. Inform consent was obtained from each participant recruited in this study.

A gynecologic examination was conducted in which cervical samples were obtained and placed into liquid-based cytology medium (PathTezt, Biocytech Corp, Perak, Malaysia). Interpretation of cervical smear was done as per the 2001 Bethesda System for reporting cervical cytology. Cervical samples were also tested for 14 types of high-risk HPV DNA (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68.) using EIA kit HPV GP HR (Diassay B.V. , Rijswijk, The Netherlands) and all positive samples were genotyped using a PCR-based assay (Inno-LiPa, Innogenetics, Ghent, Belgium).

Statistical analysis was carried out with SPSS software (IBM, Armonk, NY, USA). Descriptive statistics were used for demographic data. The associations between baseline characteristics, prevalence of abnormal cervical cytology and HR-HPVin infection were analyzed via the $\chi 2$ or Fisher exact test, as appropriate. $P<0.05$ was considered statistically significant.

Results

Of 2000 women recruited in this study, mean age and mean age at first coitus were 47.8 years and 21.6 years, respectively. One hundred and eight women (5.40%, 95%CI: 4.45-6.48) were found to be infected with HR-HPV. Table 1 displays the association of various baseline characteristics and risk of encountering HR-HPV infection. The risk of HR-HPV infection significantly correlated with age and number of partners. Age-specific prevalence of HR-HPV infection declined with age increasing. Prevalence of HR-HPV infection among women who reported to have 2 or more sexual partners was approximately 11.8% compared to 4.6% of those with single partner. No women who had never had sexual intercourse were noted to be positive with HR-HPV test compared with a rate of 5.44% of those who ever had.

Prevalence of abnormal cervical cytology was 1.95% (95%CI: 1.39-2.66). Table 2 shows the association between cervical cytology results and prevalence of HR-HPV infection. As shown, risk of HR-HPV infection was directly associated with the severity of abnormal cytology results. Most case smears of HSIL or higher tested positive (89.5%).

Table 3 displays the distribution HR-HPV subtypes among 108 women positive for HR-HPV test. Singly or in combination, the common genotype was HPV 52 (17.6%). The others in descending order included HPV 16 (14.81%), HPV 58 (13.89%), HPV 33 (11.11%), HPV 51 (11.11%), and HPV 56 (9.26%), whereas each of the remaining HR-HPV subtypes was observed in less than 10%. HPV 18 was found in only 5.6% of cases. Together, HPV 16/18 was noted in approximately 20.4% of cases. Eighteen(16.67%)women were positive with multiple subtypes of HR-HPV. Co-infection frequently involved HPV 16 or HPV 58. None of multiple HR-HPV infection involved HPV 16 and 18.

The details of HPV subtypes among 18 women with multiple HR-HPV infection were as follows: subtypes

Table 1. Factors Associated with HR-HPV Infection (n=2,000)

Factors	Category	Number of each category	HR-HPV positive (n=108)	p value
Age (years)				0.03
	30-39	328	29(8.84)	
	40-49	830	45(5.42)	
	≥ 50	842	34(4.39)	
Number of partner				< 0.01
	1	1,742	80 (4.59)	
	≥ 2	238	28 (11.79)	
Parity number				0.15
	0	88	2 (2.33)	
	1	435	31 (7.31)	
	2	1,156	62 (5.36)	
	≥ 3	321	13 (4.05)	
Age of first coitus (years)				0.68
	15-20	1,112	62 (5.58)	
	21-30	751	44 (5.53)	
	> 30	60	2 (3.23)	
Menopausal status				0.3
	Premenopause	1,297	75 (5.78)	
	Postmenopause	703	33 (4.69)	
Current contraception				0.96
	OCPs	430	26 (6.05)	
	Others	1,570	82 (5.22)	
History of smoking				0.24
	Absent	1,398	70 (5.01)	
	Present	602	38 (6.31)	

Table 2. Association between Cervical Cytology Results and Prevalence of HR-HPV Infection (n=2,000)

Cytology results	Number of each category	HR-HPV infection (n=108)
NILM	1,961	79 (4.03)
ASC-US and LSIL	20	12 (60.0)
HSIL or Higher	19	17 (89.47)

HR-HPV, high-risk human papillomavirus; NILM, negative for intraepithelial lesion or malignancy; ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; HSIL high-grade squamous intraepithelial lesion

Table 3. Distribution of HR-HPV Subtypes among 108 Women*

HR-HPV subtypes	Number (%)
Genotype 16	16 (14.81)
Genotype 18	6 (5.55)
Genotype 31	4 (3.70)
Genotype 33	12 (11.11)
Genotype 35	2 (1.85)
Genotype 39	5 (4.93)
Genotype 45	2 (1.85)
Genotype 51	12 (11.11)
Genotype 52	19 (17.59)
Genotype 56	10 (9.26)
Genotype 58	15 (13.89)
Genotype 59	3 (2.78)
Genotype 66	8 (7.41)
Genotype 68	3 (2.78)
Unknown	11 (10.18)

HR-HPV, high-risk human papillomavirus; *18 women infected with multiple subtypes

33+56 (22.22%), 51+68 (11.11%), 16+51 (5.56%), 16+58 (5.56%), 16+33+51 (5.56%), 16+33+66 (5.56%), 16+58+59 (5.56%), 31+56 (5.56%), 31+58 (5.56%), 33+58 (5.56%), 39+58 (5.56%), 51+58 (5.56%), 52+66 (5.56%), and 58+66 (5.56%).

Discussion

In this study, we evaluate the background prevalence and distribution of HR-HPV subtypes which is crucialfor designing and implementing area-specific approach. Prevalence of HR-HPV infection in this study was 5.4%. Risk of HR-HPV infection significantly associated with age and number of sexual partners. The five most common genotypes were HPV 52 (17.6%), HPV 16 (14.81%), HPV 58 (13.89%), HPV 33 (11.11%), and HPV 51 (11.11%).

Although the overall prevalence of HR-HPV infection in the present study (5.4%) was broadly comparable to a range of 6.2%-10.0% reported previously in Asian population (Chansaenroj et al., 2010; Swangvaree et al., 2010; Liu et al., 2011; Kim et al., 2012; Chen et al., 2012; Sui et al., 2013; Akcali et al., 2013), an appealing result was the notably high prevalence of HPV 52 and HPV 58 and low prevalence of HPV 16 and 18. Together, HPV 52/58 and HPV 16/18 were found in approximately 31% and 20.5% of cases, respectively, singly or in combination. Not surprisingly, the relatively high frequencies of HPV 52 and 58 were also noted in the study evaluating HPV genotyping in cervical cancer among the Northern Thai women. Approximately 18% of case specimens in this study tested positive for HPV 52/58(Siriaunkgul et al., 2008).Similarly, an extraordinarily high prevalence of HPV 52/58 was observed in Southern Chinese women (Liu et al., 2011; Chen et al., 2012). Thus, finding an extraordinarily high prevalence of HPV 52/58 but a relatively low prevalence of HPV 16/18 among this populationis relevant for estimating and counseling the potential efficacy of type-specific, prophylactic HPV vaccine. Further studies determining role of HPV 52/58 genotyping in screening approach and impact of these two common oncogenic HPV on colposcopic appearance are also warrant.

Our finding along those with previous studies reported that prevalence of HR-HPV infection was inversely associated with age (Chansaenroj et al., 2010; Swangvaree et al., 2010; Liu et al., 2011; Kim et al., 2012; Chen et al., 2012; Sui et al., 2013). In this study, prevalence of HR-HPV infection decreased from 8.84% at the age of 30-39 years to 5.42% and 4.39% at the age of 40-46, and 50 or older, respectively. Interestingly, some studies were able to demonstrate a second peak prevalence of HPV infection among older women (Chansaenroj et al., 2010; Chen et al., 2012), which might theoretically be the results of reactivation of latent infections due to age-related immunity impairment (de Sanjose et al., 2007). However, the actual mechanisms and consequences of encountering HR-HPV positive among older women remain unknown.

HPV infection is sexually transmitted disease. The association between sexual risky behavior and risk of HR-HPV infection therefore is anticipated. In study by Sui et al. (2013), age of first marriage, lifetime number of sexual partner were significant independent risk factors for HR-HPV infection. Women who had first coitus at age of 15 or younger were approximately 4-time more likely to have HR-HPV infection as compared with those at age of 25 years or older. Additionally, women reported to have 3 or more sexual partner carried a 4-fold increased risk of HR-HPV infection. Also, an increased risk of HR-HPV infection among women with history of multiple sexual partners was noted in a recent population-based survey among Southern Chinese women (Liu et al., 2011). In our study, prevalence of HR-HPV infection among women with 2 or more sexual partners was approximately 11.8% which was clearly higher than that of 4.6% among women with single partner.

In this study, prevalence of HR-HPV positivity increased with the severity of smear interpretation. Only 4% of women with normal smears had HR-HPV infection compared to around 60% and 90% of those with smears revealing ASC-US/LSIL and HSIL or higher, respectively. In previous study from Thailand, approximately 31%, 50% and 62.5% of women with ASC-US, LSIL, and HSIL smears, respectively had positive HR-HPV test(Chansaenroj et al., 2010). In a study from Republic of Korea, prevalence of HR-HPV infection were 6% of women with normal cytology, 50% for ASC-US, 74% for LSIL, and 87% for HSIL (Kim et al., 2012). The direct association of HR-HPV infection and severity of abnormal cervical cytology results is the basis information when considering HR-HPV test as a triage of women with abnormal cervical cytology results.

In conclusion, prevalence of HR-HPV infection in our setting was 5.4%. Risk of HR-HPV infection significantly correlated with age and number of partners. Singly or in combination, the common genotype was HPV 52 (17.6%), followed by HPV 16 (14.81%), HPV 58 (13.89%), HPV 33 (11.11%), HPV 51 (11.11%), and HPV 56 (9.26%). HPV 18 was found in only 5.6% of cases

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