RESEARCH ARTICLE

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Prevalence of High-Risk HPV Detection and HPV Vaccination in Cervical Cancer Screening During the HPV Vaccination Era at Siriraj Hospital – Thailand's Largest National Tertiary Referral Center

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Abstract

Objective: To investigate the prevalence of high-risk (HR) human papillomavirus (HPV) detection and HPV vaccination among women undergoing cervical cancer screening during the HPV vaccination era at Siriraj Hospital – Thailand's largest national tertiary referral center. **Methods:** This prospective cross-sectional study was conducted at our center's outpatient gynecology clinic during September-December 2021. Women aged ≥18 years with no previous hysterectomy, no history of preinvasive or invasive cervical cancer, and no current pregnancy who visited for cervical cancer screening were eligible for enrollment. Women with abnormal vaginal discharge/bleeding, and specimens with inadequate cellularity were excluded. We collected sociodemographic data, history of HPV vaccination, cervical cytology results, and high-risk HPV testing results. Reverse transcription polymerase chain reaction was used to determine HPV genotype. **Results:** A total of 216 women (mean age: 41.7 years (range: 25-65), 75.9% premenopausal) were enrolled. Twenty of 216 (9.3%) women tested positive for HR-HPV, and 15 of 216 (6.9%) women had been previously vaccinated for HPV. The most common HPV genotypes detected were Group B infection (HPV 35/39/51/56/59/66/68) (38.9%), followed by HPV16 (27.78%), Group A infection (HPV 31/33/52/58) (27.8%), and HPV18 (5.56%). No HPV45 infection was detected. The detection rate of cytologic abnormalities was 4.16%. Three-quarters (77.8%) of patients with cytologic abnormalities were HR-HPV positive. **Conclusion:** Among the 216 women who underwent cervical cancer screening in this study, there was a 9.3% prevalence of HR-HPV infection, and a 6.9% prevalence of HPV vaccination. Among the 15 vaccinated women, 2 tested positive for HPV16 (1 normal cytology, 1 abnormal cytology).

Keywords: Prevalence- high-risk HPV detection- HPV vaccination- cervical cancer screening

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Introduction

Cervical cancer screening is considered the most effective cervical cancer prevention method. The age-standardized incidence of cervical cancer has declined worldwide from 15.2 cases/100,000 females in 2008 to 13.3 cases/100,000 females in 2020, and most new cases were reported from less-developed countries [1, 2]. Persistent HR-HPV infection is a leading cause of preinvasive/invasive cervical cancer [3]. The 3 most commonly used screening methods are cytology, HR-HPV DNA test, and VIA. Of these, VIA is an attractive screening option in low resource settings [4, 5]. HPV vaccination is also regarded to be a highly effective cervical cancer prevention strategy [6, 7]; however, the cost of HPV vaccine is high in Thailand and some are unaware, so few women are vaccinated.

Several studies conducted at our center to determine and compare the effectiveness of our center's proprietary Siriraj liquid-based solution for both cytology and HPV DNA testing for cervical cancer screening revealed both its comparative effectiveness and superior cost-effectiveness [8-10]. Accordingly, our proprietary solution is now used for both tests since June 2022.

The primary aim of this study was to investigate the prevalence of high-risk HPV detection and HPV vaccination among women undergoing cervical cancer screening during the HPV vaccination era at Siriraj Hospital – Thailand's largest national tertiary referral center. Our secondary objective was to compare cytologic results between those negative for and those positive for HR-HPV, and to determine the proportion of each identified HPV genotype for each cytologic finding.

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Materials and Methods

This prospective cross-sectional study was conducted during September-December 2021. Women aged ≥18 years with no previous hysterectomy, no history of preinvasive/invasive cervical cancer, and no current pregnancy who visited for cervical cancer screening were eligible. Women with abnormal vaginal discharge/bleeding, and specimens with inadequate cellularity were excluded. The study protocol was approved by our centers IRB (COA number Si222/2021), and all patients provided written informed consent.

Cervico-vaginal specimens collected via Ayre spatula and cervical brush were immediately immersed in 10 ml of Siriraj liquid-based solution. Specimens were separated into 2 portions (8 ml for cytology, and 2 ml for HPV test). For cytology, slides were stained with Papanicolaou stain. The Bethesda System 2014 was used for cytologic interpretation, as follows: negative for NILM, ASCUS, LSIL, HSIL, ASC-H, SCC, AGC, or adenocarcinoma [11].

The Alinity m HR HPV assay (Abbott, Abbott Park, IL, USA) was used for HR-HPV testing. This RT-PCR technique targets the L1 region of 14 high-risk genotypes. Result reporting was HPV16, HPV18, and HPV45, with 11 other HR-HPV genotypes reported in two aggregates, as follows: HPV31/33/52/58 (Group A), and HPV35/39/51/56/59/66/68 (Group B) [12].

Results

Patients

A total of 216 women (mean age: 41.7 years (range: 25-65), 75.9% premenopausal) were enrolled. Other baseline sociodemographic characteristics of subjects are shown in Table 1.

History of HPV vaccination

Fifteen of 216 (6.9%) study women had previously received HPV vaccination, and 2 of those 15 women tested positive for HPV16.

Cervical cytology

Cytologic abnormalities were detected in 4.16% of study women. The cytologic findings are presented in Table 2.

Table 1. Baseline Patient Sociodemographic Characteristics (N=216)

Characteristics	Mean±SD or n (%)
Age (years)	41.73±11.05
Premenopausal status	164 (75.9%)
Postmenopausal status	52 (24.1%)
Marital status	
Single	57 (26.4%)
Married	151 69.9%)
Divorced	7 (3.2%)
Widowed/separated	1 (0.5%)
Parity	
0	85 (39.4%)
1	62 (28.7%)
≥2	69 (32.0)
Contraception	
None	103 (47.7%)
Hormonal methods	64 (29.6%)
Nonhormonal methods	49 (22.7%)
Occupation	
Unemployed	43 (19.9%)
Employed	173 (80.1%)
Comorbidity	
No	153 (70.8%)
Yes	63 (29.2%)

Abbreviation: SD, standard deviation

Table 2. Cytologic Findings Compared between the Negative for and Positive for HR-HPV Groups, and the Proportion of each Identified HPV Genotype for each Cytologic Finding (N=216)

Cytologic finding	HR-HPV		HPV genotype
type (%)	Negative (n=196) n (%)	Positive (n=20) n (%)	
NILM	194 (93.7%)	13 (6.3%)	HPV16 (23.1%) HPV18 (7.7%) Group A (15.4%) Group B (38.5%) HPV16 + Group A (7.7%) HPV16 + Group B (7.7%)
ASCUS	2 (40.0%)	3 (60.0%)	HPV16 (33.3%) Group A (33.3%) Group B (33.3%)
LSIL	0 (0.0%)	1 (100%)	Group B (100%)
HSIL	0 (0.0%)	1 (100%)	HPV16 (100%)
ASC-H	0 (0.0%)	1 (100%)	Group A (100%)
AGC	0 (0.0%)	1 (100%)	Group A (100%)

Abbreviations: AGC, atypical glandular cells; ASC-H, atypical squamous cells cannot exclude HSIL; ASCUS, atypical squamous cells of undetermined significance; Group A: the aggregate of HPV31/33/52/58; Group B, the aggregate of HPV35/39/51/56/59/66/68; HR-HPV, high-risk human papilloma virus; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; NILM, negative for intraepithelial lesion or malignancy

HR-HPV detection relative to cytology

Of the 20 (9.26%) who tested positive for HR-HPV DNA, 18 were premenopausal, and 18 had single infection. Cytologic findings compared between the negative for and positive for HR-HPV groups, and the proportion of each identified HPV genotype for each cytologic finding are shown in Table 2.

HPV vaccination and abnormal cervical cytology

Among the 15 vaccinated women, 1 had ASCUS cytology with coexisting positive HPV16. The other 14/15 women had NILM cytology. However, 1 of the 14 women with NILM cytology was positive for HPV16. Both of these women required colposcopic examination.

Discussion

After cervical cancer screening, HPV vaccination is considered the second most effective method for preventing cervical cancer [6, 7]; however, only 6.9% of our study women had been vaccinated for HPV, which is lower than other reports [13-15]. This may be explained by the high cost of the vaccine in Thailand. In this study, we did not collect data specific to sexual experience or timing of vaccination, and 2 of 15 previously vaccinated women were HPV16 positive. For the best result, HPV vaccination is recommended before sexual exposure. The Royal Thai College of Obstetricians and Gynecologists recommends that cervical cancer screening start from 25 years of age, which is the same as the recommendations from the U.S. Preventive Services Task Force and American Cancer Society [16, 17].

Our cytologic abnormality detection rate was 4.16%, which is consistent with our previous reports [8, 9]. Consistent with previous studies [18-20], ASCUS was the most common cytologic abnormality among HR-HPV positive women, and colposcopy was performed for further investigation.

Among NILM cases, HR-HPV was found in 6.28%, and nearly half (46.15%) required colposcopy. The number of NILM cases with positive HR-HPV is consistent with other reports from Thailand [21-23]. When using only HR-HPV results for screening, 9.26% of study women tested positive for HR-HPV DNA. Supporting reported variation in results, Kantathavorn, [23] reported a 6.4% rate in Thai women living in Bangkok or Pathum Thani Province, Khoo, [24] reported 7.2% in Malaysian women, and Kombe Kombe, [25] reported 9.4-30.9% in their review article. Our rate of positive HR-HPV is similar to those reported from other Thai studies [21, 22]. The prevalence of HPV positive result was higher in known abnormal cervical cytology than in general population. Song, [26] reported a prevalence of HR-HPV of 32% in women with abnormal cervical cytology in China, and Boonthum, [27] reported a prevalence of 41.5% in women with abnormal cervical cytology in Thailand.

The most commonly found HPV genotype in this study was group B infection, followed by HPV16 infection, which is consistent with previous study [22]. In contrast, Kantathavorn, [23] reported HPV52 (in Group A in this study) to be the most frequent (1.6%), followed by HPV16 (1.4%). Therefore, the results of this study indicate that the currently available commercial HPV vaccine cannot reliably prevent the most common HPV genotype. Since HPV test positivity and genotype distribution vary by region, region-specific vaccines need to be developed to optimize immunity.

Limitations

The limitations of this study include its single-center design, the fact that we did not report the prevalence of each identified genotype (we grouped some genotypes: Groups A and B), and the fact that we didn't collect information specific to sexual experience or timing of HPV vaccination.

In conclusion, among the 216 women who underwent cervical cancer screening in this study, there was a 9.3% prevalence of HR-HPV infection, and a 6.9% prevalence of HPV vaccination. Among the 15 vaccinated women, 2 tested positive for HPV16 (1 normal cytology, 1 abnormal cytology). The most prevalent abnormal cytology in both positive and negative HR-HPV was ASCUS. The most prevalent HPV genotypes were HPV16 and Group B.

Author Contribution Statement

P.C. analyzed and interpreted the patient data regarding the cytological diagnosis and HPV results and was a major contributor in writing the manuscript. S.L. reviewed the cytological diagnosis of cervical cancer screening, and C.A. performed HR-HPV assay. All authors read and approved the final manuscript.

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This study was not approved by any scientific body and was not a part of an approved student thesis.

The study protocol was approved by Siriraj IRB (COA number Si222/2021), and all patients provided written informed consent.

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Abbreviations

AGC, atypical glandular cells

ASC-H, atypical squamous cells cannot exclude HSIL

ASCUS, atypical squamous cells of undetermined significance

COA, certificate of approval

DNA, deoxyribonucleic acid

Group A, the aggregate of HPV 31/33/52/58
Group B, the aggregate of HPV 35/39/51/56/59/66/68
HPV, human papillomavirus
HR, high-risk
HR-HPV, high-risk human papillomavirus
HSIL, high-grade squamous intraepithelial lesion
IL, Illinois
IRB, institutional review board
LSIL, low-grade squamous intraepithelial lesion
ml, milliliter
NILM, intraepithelial lesion or malignancy
RT-PCR, reverse transcription polymerase chain reaction
SCC, squamous cell carcinoma
SD, standard deviation
VIA, visual inspection with acetic acid

Conflict of interest

All authors declare no personal or professional conflicts of interest, and no financial support from the companies that produce and/or distribute the drugs, devices, or materials described in this report.

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