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Prevalence of Cervical High-risk Human Papilloma Viral Infection in Pregnant Women at HRH Maha Chakri Sirindhorn Medical Center, Thailand

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ABSTRACT

Objectives: To determine the prevalence of high-risk human papilloma viral (HR-HPV) infection and the factors associated with HR-HPV infection among Thai pregnant women.

Materials and Methods: This cross-sectional study was conducted at the HRH Princess Maha Chakri Sirindhorn Medical Center from May 1, 2022 to January 31, 2023. The data were collected through primary HPV testing, liquid-based cytology (LBC), and a questionnaire.

Results: Overall, 188 pregnant women participated in the study. The mean age was 28.91 years old. The prevalence of HPV infection was 12.7% (24/188), and the two most common types were HPV 52 (6/188, 3.1%) and HPV 16 (5/188, 2.66%). No case of HPV type 18 infection was detected. Abnormal cervical cytology smears were detected in 21 samples (11.17%). The women who had multiple partners had a significantly higher risk of HR-HPV infection compared to the group who had only a single partner ($p < 0.05$).

Conclusion: The prevalence of HR-HPV infection during pregnancy in Thai women was 12.7%. Having multiple partners was found to be the greatest risk factor in this study. Primary HPV testing at a prenatal visit may be an option to improve screening coverage and could be considered in future cervical cancer screening programs.

Keywords: human papillomavirus (HPV), cervical cancer, screening, pregnancy, prevalence.

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การศึกษาความชุกของการติดเชื้อเอชพีวีความเสี่ยงสูงที่ปากมดลูก ในสตรีตั้งครรภ์ที่ศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดา ฯ สยามบรมราชกุมารี

มนัสชัย กุลพรศิริกุล, เอื้อมพร ศรีสนธิ์, วิภาดา เหล่าสุขสถิตย์, ฐานิตรา ตันติเตมิท

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาความชุกของการติดเชื้อเอชพีวีความเสี่ยงสูงที่ปากมดลูก และปัจจัยเสี่ยงต่างๆของการติดเชื้อเอชพีวีความเสี่ยงสูง ในสตรีตั้งครรภ์ชาวไทย ที่มาฝากครรภ์ที่ศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดาฯ สยามบรมราชกุมารี มหาวิทยาลัยศรีนครินทรวิโรฒ*

วัสดุและวิธีการ: *งานวิจัยแบบภาคตัดขวาง เก็บข้อมูลจากสตรีตั้งครรภ์ที่มาฝากครรภ์ที่ศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดา ฯ สยามบรมราชกุมารี มหาวิทยาลัยศรีนครินทรวิโรฒ ตั้งแต่วันที่ 1 พฤษภาคม 2565 ถึง 31 มกราคม 2566 โดยการตรวจคัดกรองมะเร็งปากมดลูกด้วยวิธีการตรวจหาเชื้อไวรัสเอชพีวีชนิดความเสี่ยงสูง (Primary HPV testing), การตรวจด้วยวิธีทางเซลล์วิทยาชนิด liquid-based cytology และการตอบแบบสอบถาม*

ผลการศึกษา: *มีสตรีตั้งครรภ์เข้าร่วมการศึกษา 188 ราย อายุเฉลี่ย 28.91 ปี พบความชุกของการติดเชื้อไวรัสเอชพีวีชนิดความเสี่ยงท่ากับ ร้อยละ 12.7 (24/188) เชื้อไวรัสสองชนิดที่พบมากที่สุดคือเอชพีวี 52 (6/188, ร้อยละ 3.1) และเอชพีวี 16 (5/188, ร้อยละ 2.66) การศึกษาครั้งนี้ไม่พบการติดเชื้อเอชพีวี 18 สำหรับการตรวจทางเซลล์วิทยาพบความผิดปกติทั้งหมด 21ราย (ร้อยละ11.17) นอกจากนี้ยังพบว่าการมีประวัติมีคู่นอนหลายคน สัมพันธ์กับการติดเชื้อไวรัสเอชพีวีชนิดความเสี่ยงสูง อย่างมีนัยสำคัญทางสถิติเมื่อเทียบกับการมีคู่นอนคนเดียว ($p < 0.05$)*

สรุป: *ความชุกของการติดเชื้อเอชพีวีความเสี่ยงสูงในสตรีไทยที่ตั้งครรภ์พบร้อยละ 12.7 และประวัติการมีคู่นอนหลายคนมีความสัมพันธ์กับการติดเชื้อเอชพีวีชนิดความเสี่ยงสูงในสตรีตั้งครรภ์ การตรวจหาเชื้อไวรัสเอชพีวีในระหว่างฝากครรภ์ทำให้การตรวจคัดกรองมะเร็งปากมดลูกมีความครอบคลุมมากขึ้น และอาจจะพิจารณาเป็นทางเลือกหนึ่งสำหรับแนวทางการป้องกันมะเร็งปากมดลูกในอนาคต*

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Introduction

Cervical cancer is the primary cause of cancer-related deaths among women in low- to middle-income countries. It is the second most common cancer with a mortality rate of 7.4 per 100,000 among women in Thailand[1]. Although it is preventable through proper screening, two-thirds of women aged 30–49 have never undergone screening for cervical cancer[2]. Approximately 50% of Thai women have not taken part in a screening program for cervical cancer[3]. Infection with high-risk human papillomavirus (HR-HPV) plays an important role in the development of cervical cancer[4]. Several studies have reported that primary human papillomavirus (HPV) testing has higher sensitivity than cytology-based methods and could be expected to improve the detection rate of high-grade cervical lesions[4-6]. This method is considered the primary screening option in Thai women aged 30–65 years old.

In 2020, the mean age of childbearing women in Thailand was 27.3 years old, with a high incidence of cervical precancerous lesions[7]. As pregnant women usually adhere to medical follow-up, cervical cancer screening during the antenatal period represents an interesting option to target young women who do not attend regular screening programs and is thus recommended in many developed countries. Some health facilities in Thailand perform cervical cancer screening during pregnancy, but most of them rely on cytologic testing, which often involves difficult evaluations due to hormone-induced changes in the cervix[8]. Therefore, most clinicians prefer to do a Pap smear at 6 weeks postpartum[9]. From a survey of our center, less than 50% of women do not attend a postpartum visit. There have been no studies on primary HPV testing among pregnant women in Thailand yet. However, a previous study reported that abnormal cervical cytology results were found in approximately 4%–7% of Thai pregnant women[10, 11]. Studies from other countries have reported high-risk HPV prevalent rates among pregnant women ranging from 13%–20%[12-14]. Many factors could increase the risk of HPV infection during pregnancy, for example, young age, the number of lifetime sexual partners, and the presence of abnormal cervical cytology[13, 15]. This study aimed to determine the prevalence and factors associated with high-risk human papilloma viral infection among Thai pregnant women in order to assess the feasibility of including a primary HPV screening program during antenatal care.

Materials and Methods

This cross-sectional study was conducted at the HRH Princess Maha Chakri Sirindhorn Medical Center between May 1, 2022, and January 31, 2023. The participants were pregnant women who visited the antenatal care clinic before 28 weeks of gestational age. The inclusion criteria were pregnant women aged over 20 years old, who had an intrauterine pregnancy confirmed by ultrasound. The exclusion criteria were pregnant women who had been screened for cervical cancer within the past year; had a history of abnormal cervical cancer screening, precancerous, or cancerous of cervix; had experienced abnormal vaginal bleeding; who were unable to be on dorsal lithotomy; or who did not understand the Thai language.

The sample size was calculated based on a prevalence of HPV infection in pregnancy of 13.4% from a pilot study. After calculation, a total of 188 participants were included in the study, including cover for a 5% loss. This study was approved by the Ethics Committee of Srinakharinwirot University (SWUEC/E/M-012/2565).

After obtaining informed consent, the participants were asked to complete a questionnaire about their demographics, pregnancy history, cervical cancer screening history, HPV vaccine history, and risk factors for cervical cancer. Cervical cancer screening was conducted using both primary HPV testing and liquid-based cytology (LBC). Specimens were collected from the ectocervix using a Cytobrush in 5 rounds and were stirred into a transport medium solution (Cellprep®, Seongnam, Korea). All the specimens were sent to the Virology Department for primary HPV testing and then forwarded to the Pathology Department for a single pathologist to

report the cytology results according to the Bethesda 2001 reporting system. The HPV results were blinded to the clinical status and cytologic results. HPV testing was performed using a high-risk HPV deoxyribonucleic acid (DNA) diagnostic kit for identification of the HPV genotypes (Sansure Biotech Inc, Hunan, China). This diagnostic kit is an in vitro nucleic acid amplification test for the detection of high-risk human papillomavirus (types 16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68) present in exfoliated cells from a female cervix. The test results can be used for the diagnosis of a high-risk HPV infection. The participants who had HPV type 16 or 18 infection and other high-risk HPV infections with an abnormal cervical cytology (atypical squamous cells of undetermined significance (ASC-US) or more) were referred to a gynecologic oncologist for colposcopic examination.

The patients' demographic data, obstetric profile, history of cervical cancer screening, and risk of cervical cancer were obtained using a questionnaire. Descriptive statistics were used to describe various characteristics, and reported as the mean, frequency, percentage, and standard deviation. The chi-square test was performed to analyze associations between the demographic data and HPV prevalence. The p value was set at 0.05 for statistical significance. All the data were analyzed using Stata version 14.1 For Mac.

Results

Overall, 188 pregnant women were enrolled in this study. The demographic characteristics of these are presented in Table 1.

Twenty-four pregnant women were infected with HR-HPV, representing a prevalence of 12.7% of all pregnant women (Table 2). The two most common types were HPV 52 (6 cases, 3.1%) and HPV 16 (5 cases, 2.6%). Two cases had multiple HPV infections, which were HPV 51, 53, 68, and 52, 53. No case of HPV type 18 infection was detected in this study.

Table 1. Demographic characteristics of the study population (n = 188).

Characteristics	Number (%), mean ± SD
Age (mean ± SD)	28.91 ± 4.95
20 – 29	116 (61.7%)
30 – 41	72 (38.3%)
Gravidity	
Nulliparous	69 (36.7%)
Multiparous	119 (63.3%)
Gestational age at examination (weeks)	12.29 ± 4.15
1st trimester (< 14 weeks)	117 (62.23%)
2nd trimester (≥ 14 weeks)	71 (37.77%)
Education	
< Bachelor's degree	111(59.04%)
≥ Bachelor's degree	77(40.96%)
Income per month (THB)	25,440.43 ± 14794.97
< 20,000	67 (35.64%)
≥ 20,000	121 (64.46%)
History of cervical cancer screening	
No	89 (47.34%)
Yes	99 (52.66%)
History of contraception	
No	65 (34.57%)
Yes	123 (65.43%)
Age at first intercourse (mean ± SD)	19.62 ± 3.82
< 20	96 (51.06%)
≥ 20	92 (48.94%)
Number of partners (mean ± SD)	1.69 ± 0.955
1	106 (56.38%)
≥ 2	82 (43.62%)
History of smoking	
No	186 (98.94%)
Yes	2 (1.06%)
History of HPV vaccine	
No	188 (100%)
Yes	0 (0%)

SD: standard deviation, THB: Thai baht, HPV: Human papillomavirus

Table 2. Prevalence of HPV infection.

HPV types	Number	%
Positive HPV 16	5	2.6
Positive HPV 18	0	0
Other high-risk types	19	10.1
31	2	
39	3	
45	1	
51	1	
52	5	
53	1	
56	1	
58	1	
59	1	
66	1	
52, 53	1	
51, 53, 68	1	
Total	24	12.7

HPV: Human papillomavirus

The results from the liquid-based cytology (LBC) tests and the relationship to HPV status are shown in Table 3. Abnormal cervical cytology smears were detected in 21 samples (11.17%), consisting of 16 (8.5%) with atypical squamous cells of undetermined significance (ASC-US) and five (2.6%) with a low-grade squamous intraepithelial lesion (LSIL). Most of the cases with abnormal cytology were associated with high-risk HPV infection (85.7%). Twenty-five percent of the participants with high-risk HPV infection had normal cervical cytology (6 cases). Twenty cases were referred for colposcopic examination, while only one case was suspected of a high-grade lesion and a cervical biopsy was done during pregnancy. The final pathology of that latter case reported cervical intraepithelial neoplasia 1 (CIN1).

Table 3. Results of cervical cytology in relation to HPV status.

LBC	High-risk HPV infection			
	Undetected	Type 16	Other HR	Total
NILM	161	2	4	167
ASC-US	3	2	11	16
LSIL	0	1	4	5
HSIL	0	0	0	0

LBC: liquid based cytology, HR: high risk, HPV: human papillomavirus.

Table 4 presents a comparison of the patients' characteristics and risk factors of cervical cancer between pregnant women without high-risk HPV infection and those with high-risk HPV infection. We found that having multiple partners was the only factor associated with an increased risk of HR-HPV infection during pregnancy (p-value < 0.05).

Table 4. Comparison of the characteristics between pregnant women without high-risk HPV infection and with high-risk HPV infection.

Characteristics	Number (%)	No HR-HPV infection	HR-HPV infection	p value
Age				0.592
20 – 29	116 (61.7%)	100 (60.98%)	16 (66.67%)	
30 – 41	72 (38.3%)	64(39.02%)	8 (33.33%)	
Gravidity				0.589
Nulliparous	69 (36.7%)	59 (35.98%)	10 (41.67%)	
Multiparous	119 (63.3%)	105 (64.02%)	14 (58.33%)	
Gestational age at examination (weeks)				0.076
14 weeks	117 (62.23%)	106 (64.63%)	11 (45.83%)	
≥ 14 weeks	71(37.77%)	58 (35.37%)	13 (54.17%)	
Education				0.159
< Bachelor's degree	111(59.04%)	100 (60.98)	11 (45.83%)	
≥ Bachelor's degree	77(40.96%)	64 (39.02%)	13 (54.17%)	
Income per month (THB)				0.478
< 20,000	67 (35.64%)	60 (36.59%)	7 (29.17%)	
≥ 20,000	121 (64.46%)	104 (63.41%)	17 (70.83%)	
History of cervical cancer screening				0.248
No	89 (47.34%)	75 (45.73%)	14 (58.33%)	
Yes	99 (52.66%)	89 (54.27%)	10 (41.67%)	
History of contraception				0.551
No	65 (34.57%)	58 (35.37%)	7 (29.17%)	
Yes	123 (65.43%)	106 (64.63%)	17 (70.83%)	
Age at first intercourse				0.446
< 20	96 (51.06%)	82 (50.0%)	14 (58.33%)	
≥ 20	92 (48.94%)	82 (50.0%)	10 (41.67%)	
Number of partners				0.015
1	106 (56.38%)	98 (59.76%)	8 (33.33%)	
≥ 2	82 (43.62%)	66 (40.24%)	16 (66.67%)	
History of smoking				1.000
No	186 (98.94%)	162 (98.78%)	24 (100%)	
Yes	2 (1.06%)	2 (1.22%)	0 (0.0%)	
History of HPV vaccine				1.000
No	188 (100%)	164 (100.0)	24 (100.0)	
Yes	0 (0%)	0	0	

HR: high risk, HPV: human papillomavirus, THB: Thai baht

Discussion

This study found that the prevalence of HR-HPV-infected pregnant women was 12.7% in our cohort, while the prevalence from previous studies in other countries varied from 13%–20%[12-14]. One study from India collected samples from condoms used to cover the vaginal sonography probe during patients' first-trimester visits, and found a prevalence of almost 40%, which was much higher than in our study[16]. A study from Lithuania reported a prevalence of HR-HPV infection in pregnancy of 9.3%, which was obtained by collecting cervicofacial washing fluid during pelvic examinations in the first and third trimesters[17]. Another study from France collected samples from pregnant women with a gestational age of less than 24 weeks by routine Pap smear and HPV testing and found an HR-HPV prevalence of 20%[14]. The difference in prevalence in various studies could possibly be explained by the differences in the geographical area, HPV detection assay used, sample collection method, and timing of sample collection. The differences in HR-HPV infection rates during pregnancy have also been studied and it was found that the prevalence of HPV infection in the first trimester tends to be higher than in the second trimester[13,18]. With respect to the HR-HPV genotypes, the most common genotype was HPV 52 followed by HPV16. This finding was consistent with a previous study from a large cohort of the general population in Thailand[19]. However, there were no cases in our study infected with HPV18, which is the second most common type worldwide[20]. The low prevalence of this genotype has also been reported in previous Thai studies[19, 21, 22].

The prevalence of abnormal cytological smears in pregnant women in our study was 11.7%, which is higher than in the past studies in Thailand (4%–7%)[10, 11]. The sociodemographic characteristics of the pregnant women in those earlier studies were similar to those in our study. This suggests that the rate of abnormal cytology and preinvasive cervical cancer seems to be increasing. Prenatal care provides an opportune time for screening. Another explanation for the difference in the prevalence of cervical smears among these studies could be the poor reproducibility and limited accuracy of cytological diagnoses[23, 24]. One study conducted in a general Thai population reported that agreement between skilled observers, at the level of tests requiring diagnostic follow-up or not, was only moderate. The discrepancies were greatest for the minor degrees of cytological abnormality in the Bethesda classification[24]. The interpretation of cytologic specimens is more difficult in pregnancy, as the hormonal changes, Aris–Stella reaction, and decidualization in pregnancy result in changes in epithelial cells that simulate malignancy and may cause confusion[8]. For this reason, we recommend HR-HPV testing as the preferred approach in pregnant women.

We found that women with multiple partners had a significantly increased risk of HR-HPV infection in pregnancy. A previous meta-analysis suggested that young pregnant women, especially those aged < 25 years old, were more susceptible to HPV infection[13]. Our study analyzed the prevalence of HPV in different age groups. However, these results need to be verified by further study.

Recently in our country, there has been a movement toward the implementation of HPV testing to precede cytology-based screening programs. It is thus interesting to study HPV-based screening in the target population during pregnancy. To the best of our knowledge, this is the first prospective study in Thailand to report the prevalence of HPV infection during pregnancy. We also reported the prevalence of cervical cytology and the factors associated with HPV infection. The limitations of this study included our small sample size and the fact that only one-time testing was performed in the first half of pregnancy, and we did not repeat HPV testing before delivery or at the postpartum visit to assess HPV clearance. The changes of HPV infection in each trimester and at the postpartum visit have, however, been reported in several studies[13, 17, 18]. Moreover, as a result of the small number of HPV-positive women in our study,

we could not evaluate the association between maternal HPV infection and adverse pregnancy outcomes. Also, due to time constraints and as it was considered beyond the scope of the study, the results of follow-up and adherence to the screening program could not be reported. The clearance of HPV infection, maternal outcome, adherence, and cost-effectiveness of this strategy in pregnancy would be interesting to determine and might be more meaningful to study in the future.

Conclusion

In conclusion, the prevalence of HR-HPV infection during pregnancy in Thai women in our study was 12.7%. The most significant risk associated with having multiple partners was the increased risk of this infection. Our findings suggest that including primary HPV testing in a prenatal visit may be an option to improve screening coverage in Thailand.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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