



A population-based study of cervical cytology findings and human papillomavirus infection in a suburban area of Thailand



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ARTICLE INFO

Keywords:

Cervical cancer screening
HPV testing
HPV genotyping
Cervical cytology
Population-based
Thailand

ABSTRACT

Despite the high incidence of cervical cancer in Thailand, large population-based studies on cervical cytology and HPV prevalence and genotype distribution are rare. This study aimed to determine cervical cytology results and the prevalence and distribution of HPV among Thai females in Bangkhayaeng subdistrict, Pathumthani province, Thailand. Of 4681 female inhabitants, aged 20–70 years, 1523 women finally participated in the study. Cervical samples using liquid-based cytology were collected during February–August 2013 and analyzed for HPV genotype by the LINEAR ARRAY® HPV Genotyping Test (Roche, USA). All participants with abnormal cytology or HPV positivity underwent colposcopy and biopsy. Of 1523 eligible women, 4.1% had abnormal cytology including ASC-US (2.4%), LSIL (1.0%), and HSIL (0.5%). The HPV infection rate was 13.7%. The prevalences of high-risk, probable high-risk, and low-risk HPV types were 5.6%, 3.5%, and 6.8%, respectively. The most common high-risk HPV types detected were HPV-16 (1.31%), HPV-51 (1.25%), and HPV-52 (1.25%). The most common probable high-risk and low-risk HPV types detected were HPV-72 (1.51%), HPV-62 (1.38%), and HPV-70 (1.18%). The rates of CIN2–3 and cancer in this cohort were 1.4% and 0.3%, respectively. In conclusion, HPV prevalence in this study was lower than reported in studies conducted in Western countries or other Asia countries, despite the high prevalence of CIN2+ and cancer. HPV type screening results of the general population in Bangkhayaeng subdistrict were similar to those reported in other countries, with HPV-16 the most common type. However, higher frequencies of HPV-51 and HPV-52 were observed. Despite the availability of a free screening program in this area, the participation rate remains low.

1. Introduction

Per GLOBOCAN 2012, cervical cancer is the fourth most common cancer in women worldwide with 528,000 new cases reported annually (Ferlay et al., 2013). It is also the fourth most common cause of cancer death in women with 266,000 deaths occurring worldwide in 2012. Almost 70% of the global cervical cancer burden is found in less developed countries. Despite the decreasing worldwide incidence, cervical cancer remains a critical health problem in Thailand with > 8000 new cases diagnosed annually (rate, 16.7 per 100,000 persons). Additionally, it is the second most common cancer and a leading cause of cancer death in Thai women after breast cancer (Ferlay et al., 2013).

High-risk human papillomavirus (HPV) types are now recognized as a causal factor of cervical cancer (Walboomers et al., 1999). The distribution of HPV genotypes varies according to ethnic, geographic, and behavioral factors (Bruni et al., 2010). Increased understanding about

geographical distribution of HPV genotypes in Thailand may aid in development of cervical cancer control policies.

A limited number of population-based studies about cervical cytology and HPV infection in Thailand have been performed. Therefore, we conducted a study in Bangkhayaeng subdistrict, Pathumthani province to evaluate cervical cytology and HPV prevalence in all women residing in this area. A cervical cancer screening service using liquid-based cytology and HPV DNA testing was performed in all participants. Colposcopy was then performed for women with abnormal cytology results. Our study aimed to determine cytologic findings and HPV prevalence and genotype using cervical samples collected from women living in a suburban area of Thailand.

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<http://dx.doi.org/10.1016/j.gore.2017.06.003>

Received 7 March 2017; Received in revised form 14 May 2017; Accepted 2 June 2017

Available online 04 July 2017

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2. Materials and methods

2.1. Study population

This study was conducted in Bangkhayaeng subdistrict, Pathumthani province, which is close to Bangkok, during February–August 2013. The study was approved by Chulabhorn Hospital's ethical committee for human research (No. 01/2556). Gynecologic oncologists from Chulabhorn Hospital cooperated with subdistrict health officers at a Bangkhayaeng health promotion hospital to educate women about cervical cancer and the free screening program.

House-to-house recruitment of all adult women aged 20–70 years residing in this subdistrict was conducted by subdistrict health officers of the Ministry of Public Health. Cervical screening by liquid-based cytology and HPV genotyping were performed. Exclusion criteria included absence of a cervix, history of abnormal cytology or cervical intraepithelial neoplasia, cervical carcinoma, active diseases for any types of cancer during the last 5 years, or inability to receive follow-up. Women who agreed to participate provided written informed consent and received a pelvic examination by gynecologic oncologists.

2.2. Sample collection and preparation

Samples were obtained using a cytobrush by gynecologic oncologists of Chulabhorn Hospital. The brush was then placed in preservative fluid in the BD SurePath Pap test kit (BD Diagnostics-Tripath, Burlington, NC, USA) for liquid-based cytology and HPV DNA testing. Investigators performing HPV typing were blinded to cytology results. All cervical cytology slides were interpreted by standard protocol by qualified pathologists at Chulabhorn Hospital using the Bethesda 2001 system.

2.3. HPV genotyping

HPV genotyping was performed using the LINEAR ARRAY® HPV Genotyping Test (Roche Molecular System, Inc., Branchburg, NJ, USA) according to the manufacturer's protocol. This kit can identify 37 HPV types: 12 high-risk (HR) types (16/18/31/33/35/39/45/51/52/56/58/59), 8 probable high-risk (PR) types (26/53/66/67/68/70/73/82), and 17 low-risk (LR) types (6/11/40/42/54/55/61/62/64/69/71/72/81/83/84/IS39/CP6108), which are classified by oncogenic potentiality.

2.4. Diagnostic procedures

Cytologic specimens were classified by the Bethesda 2001 system into atypical squamous cells of undetermined significance (ASC-US), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL), and cancer. All women with abnormal cytology results (ASC-US or more severe) and those with any HPV types underwent colposcopy, endocervical curettage, and cervical biopsy. Biopsy of a visible lesion was then performed. For patients with no visible lesion, a random biopsy was performed. Endocervical curettage and biopsy specimens were then analyzed by qualified pathologists at Chulabhorn Hospital.

2.5. Statistical analysis

We used descriptive statistics to determine distribution and frequencies of HPV, age, and cytology results. Frequency tables were used for qualitative variables. Odds ratios (ORs) with 95% confidence intervals (CIs) were used for relative risk evaluation.

3. Results

3.1. Participation rates

Of 4681 women aged 20–70 years from Bangkhayaeng subdistrict, 1780 women (38.0%) participated. Of these, 257 women were excluded, thus 1523 women were finally enrolled in this study. The main reasons for exclusion were residence outside of Bangkhayaeng subdistrict, refusal to participate, or did not show up for appointments.

3.2. Demographic characteristics

The mean age of participants was 44.5 years (range, 20–70 years). The proportions of participants aged 20–30 years and 31–70 years were 10.9% and 89.1%, respectively. Most women (96.4%) had had sexual intercourse and reported contraception use (71.0%). Eighty-four percent was multiparous and 68% was premenopausal. Nearly half of the participants' educational level was elementary school (44.7%), followed by high school (26.9%), bachelor's degree (12.3%), and vocational school (11.9%). Only 1.9% of the cohort had an education level below the standard education level.

3.3. Prevalence of abnormal cervical cytology and HPV infection

All specimens were sufficient for sequencing. There were 1292 (84.8%) women with normal results (normal cytology/HPV-negative) and they received follow-up appointments at 5-year intervals. Twenty-three (1.5%) women had abnormal cytology/HPV-negative, 168 (11.0%) women had normal cytology/HPV-positive, and 40 (2.6%) women had abnormal cytology/HPV-positive. Women in these three groups underwent colposcopy with endocervical curettage and cervical biopsy to acquire histologic diagnoses. Fig. 1 demonstrates pathology results of these groups.

The rates of CIN2+ lesions [cervical intraepithelial neoplasia (CIN) 2–3, adenocarcinoma in situ (AIS), and carcinoma] in the abnormal cytology/HPV-negative group, normal cytology/HPV-positive group, and abnormal cytology/HPV-positive group were 0%, 7.2%, and 35.0%, respectively. Of 1523 women, CIN2–3/AIS were found in 22 women (1.4%). Invasive cervical cancer was found in four women (0.3%).

Table 1 shows the overall HPV prevalence according to cytology result and prevalences of HR-HPV, PR-HPV, and LR-HPV. Of 1523 women, 4.1% (n = 63) had abnormal cytology results including ASC-US (2.4%, n = 37), LSIL (1.0%, n = 15), and HSIL (0.5%, n = 8). Other abnormal cytology results included ASC-H, atypical glandular cell, and squamous cell carcinoma (SCC), which were each found in 0.06% (n = 1) of women.

Overall, HPV was detected in 13.7% (n = 208) of specimens. The overall prevalence of HR-HPV was 5.6% (n = 86). When classified by cytologic findings, overall HPV and HR-HPV positivity rates in the normal cytology group were 11.5% and 4.1%, respectively. For the abnormal cytology group, HPV and HR-HPV positivity rates were 63.5% and 41.3%, respectively. In the LSIL group, HPV and HR-HPV positivity rates were 93.3% and 46.7%, respectively. In HSIL and SCC groups, HR-HPV was detected in all specimens.

HPV-16 prevalence was 1.31% (n = 20), which was the most common HR-HPV type followed by HPV-51 (1.25%, n = 19) and HPV-52 (1.25%, n = 19) (Fig. 2A). HPV-18 prevalence was only 0.53% (n = 8).

Overall, HPV infection was highest in young women aged 20–30 years, which decreased with increasing age but increased again in women aged 61–70 years (Fig. 2B). HPV prevalences stratified by age were as follows: 19.3% (20–30 years), 15.5% (31–40 years), 12.0% (41–50 years), 10.0% (51–60 years), and 16.8% (61–70 years).

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