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Prevalence of HPV and Type Distribution in Southeast Asian Women Residing in Rhode Island

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Abstract

Objective: The objective of this study was to assess the prevalence of cervical high-risk HPV among Southeast Asian women and describe the distribution of the high-risk genotypes.

Methods: SE Asian women (n=57) ages 18 years and older and residing in and around the vicinity of Providence, RI were enrolled. Women were recruited at community health centers and underwent thin-prep pap smears and high-risk HPV genotyping of the cervix. All pap smears were reviewed at Women & Infants Hospital of Rhode Island by specialized gynecologic cytopathologists, and thin prep vials sent for HPV genotyping.

Results: The median age of SE Asian participants was 38 years old (range 21-63). Fifteen (26%) were married and the majority were born outside of the United States. The majority had sexual partners born outside the US (60%). High-risk HPV was detected in 14 (25.0%) women with the most common genotypes being 51 (28.6%), 52 (21.4%), 56 (21.4%), and 59 (21.4%). Of interest, HPV 16 was only reported in one woman; none had HPV 18. Co-infection with more than one HPV genotype was seen in 6 (10.7 %) women.

Conclusions: High-risk HPV is prevalent even among low risk SE Asian women residing in the north-east. However, HPV 16 was rarely identified and none of this cohort had evidence of HPV18 infection. These data demonstrate that HPV vaccination must take into account the heterogeneity of infections among different racial groups to aid in future vaccine development.

Keywords: Southeast Asian; High-risk HPV; Cervical cancer; Racial disparities

Introduction

In the United States (US) there has been a remarkable decrease in the incidence of, and mortality from, cervical cancer since the 1940s, due in large part to cervical cancer screening programs [1,2]. It is now known that cervical cancer is caused by oncogenic subtypes of the human papillomavirus (HPV) [3]. DNA testing for various serotypes of the HPV virus with cervical cytology testing has become a valuable option for both primary and adjunct screening [4]. Although screening has led to a significant decrease in cervical cancer incidence in the United States, cervical cancer remains an important cause of cancer death in women worldwide [2,5,6].

With the approval of two HPV vaccines (bivalent and quadrivalent), it is anticipated the rates of cervical cancer in the United States and eventually worldwide, will continue to decline [5,6]. These vaccines protect against high risk HPV types 16 and 18, which represent 2 of the 15 high-risk oncogenic HPV genotypes responsible for causing cervical cancer. In addition, there is some cross-protectivity against high-risk types 31 and 45 with these HPV vaccines [7]. While approximately 70% of cervical cancers in the US and Europe are caused by HPV 16 and 18, only 60% to 70% of cervical cancer are associated with those serotypes in Africa, Asia, and Latin America, with serotypes 31,35 and 45 contributing to a large portion of the disease [5,8]. More specifically, in the Philippines 15.7% of cervical cancers are caused by HPV 45 and in Latin America HPV 31 and 35 are detected in a significant proportion of cervical cancers [9]. In addition, in parts of Asia, HPV 52 and HPV 58 along with HPV 16 are the most common HPV genotypes identified [10,11]. Therefore, it is important to understand geographic variations of HPV distribution to determine the effectiveness of the HPV vaccines both globally and in the US.

In the US, cervical cancer remains a significant burden among various racial and ethnic groups. In particular, women of Southeast Asian descent have nearly twice the incidence of cervical cancer than Non-Hispanic white women [12,13,14]. While we know cervical HPV prevalence and genotypes differ substantially from one population to the next worldwide, we have limited information on racial and ethnic differences in the US [15]. In the initial vaccine trials, over 70% of the participants were from North America or Europe (although not specifically broken down by race or ethnicity) while less than 1.5% were from Asia [8].

Asians have not only been under represented in large cervical cancer screening trials, but are often evaluated as one large group despite being heterogeneous. For instance, Southeast Asian women have higher incidence of cervical cancer compared to other Asian groups, such as Pacific Islanders [16]. In addition, the most prevalent HPV genotypes may vary by country of origin as observed among

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women residing in Vietnam, Cambodia and other Asian countries [10,15,17].

Therefore, despite the advancements in prevention of cervical cancer, there is still much to be learned about the epidemiology of HPV in order to aid in future vaccine development. SE Asian women continue to be at increased risk of cervical cancer because they are less likely to undergo regular screening by pap tests in comparison to Non-Hispanic white women [1,18,19]. Additional information on the prevalence of high-risk HPV among SE Asian women in the U.S., as well as information on the genotype distribution is crucial for ensuring future vaccine development provides adequate coverage for this population. The objective of this study was to determine the prevalence of HPV high-risk genotypes among these women.

Methods

Study setting and population

A cross-sectional pilot study was performed at five community health center clinics in one New England state. Approval was obtained through a hospital institutional review board and permission was obtained by the health center administration. Approximately 50% of Southeast (SE) Asian women residing in the state received their care at these clinics. Potentially eligible women self-identified as SE Asian and presented to the clinic for routine gynecologic care.

Potentially eligible women were recruited by a health care provider for participation in the study. Study inclusion criteria were as follows: 1) 18 years or older and eligible for HPV screening as per the American Society for Colposcopy and Cervical Pathology (ASCCP)/American Congress of Obstetricians and Gynecologists (ACOG) guidelines; 2) identified as Hmong, Laotian, Cambodian, Vietnamese, or Thai descent; 3) had an intact uterine cervix; and 4) were able and willing to give informed consent with interpreter assistance as needed. Women were excluded if they: 1) were under the age of 18 or did not meet the screening guidelines; 2) had any of the three injections for the HPV vaccine series 3) had undergone hysterectomy with removal of the cervix; 4) had a history of prior pelvic radiation therapy; 5) had a history of cervical, vaginal or vulvar invasive cancer; 6) were unable to give informed consent. Eligible women were invited to enroll and informed consent was obtained in English, Hmong, Thai, Lao, Khmer, or Vietnamese.

Data collection

A self-administered paper questionnaire was given to all eligible women in the language chosen by the participant. The questionnaire included demographic questions not asked as part of the screening process, sexual history questions and questions regarding country of origin of current and past sexual partners. Participants were offered an informational pamphlet designed for SE Asian women with information on cervical cancer screening and HPV vaccination.

Cervical cytology and high-risk HPV genotyping

For all participants, cervical cytologic samples and HPV swabs were collected by a physician using the standard thin-layer cytology with a spatula/broom and endocervical brush. HPV typing was performed at the Physicians Reference Laboratory using a complex multiplex real time PCR test that simultaneously detects, types, and quantifies all 15 high risk HPV types known to cause anogenital cancer. The HPV genotyping was run using the residual ThinPrep Vial (Complete Care HPV test; Physicians Reference Laboratory, Overland Park, KS). The high risk HPV subtypes tested were: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73 and 82. The thin-layer cytology was reviewed by one of three Pathologists. In the event of an abnormal cervical cytology, participants were managed per the ASCCP/ACOG guidelines.

Measures

The outcome variables measured were high-risk HPV infection, co-infection with multiple HPV types and high-risk HPV genotype. Demographic questions included patient age, ethnicity, length of time residing in the United States, birth place and geographic history, insurance status, gravidity and parity, socioeconomic status, education. Relevant medical and surgical history as well as additional information on past cervical cancer screening and history of prior abnormal pap smears or treatments was obtained. Pap smear results and colposcopic findings were also documented.

Statistical analysis

Variables were summarized by proportions, means, medians, and ranges. Ninety-five percent confidence intervals (95% CI) were calculated as measures of statistical stability for prevalence estimates.

Results

Fifty-seven self-identified SE Asian women were recruited. The mean age of participants was 38.5 years (range 21 to 63) and 26.3% of women were married. The majority were born outside of the U.S. (84.2%), but had lived in the U.S. for a median of 21 years (0.2 to 30 years). Similarly, the majority of women had sexual partners not born in the U.S. (59.6%). The country of origin was similar for participants and their current sexual partners (Table 1).

The clinical characteristics of participants are described in Table 2. Sixteen percent of women were menopausal and only 1.8% reported tobacco use. All women reported a history of sexual activity. Seventy-five percent of women reported current sexual activity with a median of 1.5 lifetime sexual partners. All women reported only one sexual partner in the past 6 months. Only 5% reported a history of a sexually transmitted infection, including chlamydia or gonorrhea. Women had a median of 2 children and nearly 20% had a tubal ligation as their form of birth control. Sixteen percent of women were pregnant at the time of recruitment, median gestational age 14 weeks (range 8 to 19).

Forty-four percent of participants had a pap smear within the 3 years prior, while 14% of participants reported never having a pap smear or not having one in over 5 years. Approximately 21% of these patients reported a history of an abnormal pap smear, although 49% reported their most recent pap smear was normal.

Cervical cytology results

There were only 5 women with abnormal cervical cytology results: 2 ASCUS (3.6%) and 3 LGSIL (5.4%) (Table 3). One ASCUS was HPV negative the other was co infected with 35 and 56. One LGSIL was positive for high-risk type 51 and another for 56, while the third LGSIL was positive for 51, 58 and 59.

Table 1: Demographic and sexual partner characteristics.

Characteristic	Southeast Asian women
Total	N=57
	n (%)
Age (y), mean (SD)	38.5 (11.2)
Range	21 - 63
Marital status	
Single	11 (19.3)
Married	15 (26.3)
Divorced	1 (1.8)
Separated	1 (1.8)
Widowed	1 (1.8)
Missing/refused	28 (49.1)
Country of birth	
US	9 (15.8)
Cambodia	27 (47.4)
Vietnam	1 (1.8)
Laos	16 (28.1)
Thailand	4 (7.0)
If born outside of US, years living in US, median (Range)	21 (0.2 - 30)
Missing/refused	11
Language preferred	
English	23 (40.4)
Cambodian	17 (29.8)
Hmong	2 (3.5)
Laotian	11 (19.3)
Other	4 (7.0)
Current sexual partner born in the US	
Yes	10 (17.5)
No	34 (59.6)
No current sexual partner	8 (14.0)
Missing/refused	5 (8.8)
If current sexual partner was not born in US, country of origin	
Cambodia	21 (48.8)
Vietnam	2 (4.7)
Laos	14 (32.6)
Thailand	3 (7.0)
Other	2 (4.7)
Missing/refused	1 (2.3)

NOTE: Percentages may not sum to 100 due to rounding.

HPV subtyping

A total of 14 (25.0%, 95% CI: 14.4% –38.4%) participants had a high-risk HPV infection. The most common genotypes of HPV detected were HPV 51, 52, 56 and 59 followed by HPV 35, 73 then HPV 16, 5, 82 (Table 4). Nearly half (6 of 14) of the HPV infections were with more than one high-risk HPV genotype (Table 5). Two participants tested positive for 3 high-risk HPV genotypes while the other 4 participants tested positive for two high-risk HPV genotypes. HPV 16 was only found in one participant who was also positive for HPV 52. No women tested positive for HPV 18.

Discussion

In our study of SE Asian women, ages 21-63 years, we found 25% of participants had a high-risk HPV infection. The National Health and Nutrition Examination Survey from 2003-2006 reported a prevalence of high-risk HPV of 29% among comparably aged women [20,21]. This supports the theory that a higher prevalence of high-risk HPV is not the reason SE Asian women have a higher incidence of cervical cancer. It is likely due to low participation in cervical cancer prevention, as seen in our study with only 65% of participants having a pap smear in the past 3 years. Regular pap smears allow for the early detection and ultimate removal of precancerous lesions. Therefore, the lower rate of pap smear use reinforces the need for HPV vaccination among this high risk group.

Table 2: Clinical characteristics.

Characteristic	Southeast Asian women (N=57) n (%)
Pregnant	
Yes	9 (15.8)
No	48 (84.2)
Gravidity, median (range)	3 (1 - 12)
Missing	3
Parity, median (range)	2 (0- 8)
Missing	4
Contraception	
Condoms	0 (0)
Oral contraceptive pills	2 (8.3)
Intrauterine device	5 (20.8)
Depot medroxyprogesterone acetate	4 (16.7)
Patch	2 (3.5)
Tubal ligation	11 (19.3)
None/Missing	33 (57.9)
Last Pap smear	
Within past 3 years	25 (43.9)
3-5 years ago	5 (8.8)
>5 years ago	4 (7.0)
Never	4 (7.0)
Missing	19 (33.3)
If ever had a Pap, history of results	
Normal	22 (64.7)
ASCUS	1 (2.9)
LGSIL	1 (2.9)
HGSIL	0 (0)
Other	5 (14.7)
Missing	5 (14.7)
Menopause	
Yes	9 (15.8)
No	47 (82.5)
Missing	1 (1.8)
STD history	
None	46 (80.7)
Chlamydia	1 (1.8)
Gonorrhea	1 (1.8)
Other	1 (1.8)
Missing	8 (14.0)
Currently sexually active	
Yes	43 (75.4)
No	8 (14.0)
Missing	6 (10.5)
Number of lifetime partners, median (range)	1.5 (1 - 2)
Missing	53
Tobacco use	
Yes	1 (1.8)
No	52 (91.2)
Missing	4 (7.0)

NOTE: Percentages may not sum to 100 due to rounding.

Over 85% of participants in our study were born outside of the United States. Additionally, the majority of our participants had sexual partners that were also born in a SE Asian country, regardless of time spent in the U.S. Although our numbers are low because this was a pilot study, we found only one (7.1%) woman in our study infected with high-risk 16 HPV and/or 18 out of 14 women with high-risk HPV. In our sample, HPV 51 was the most common high-risk HPV genotype among SE Asian women, followed by HPV genotypes 52, 56 and 59. Similarly, a study performed among married women in Viet Nam reported HPV 16 and/or 18 in only 7% of women, with others being infected with HPV 58, 52, 35 and 45. Vu et al., [22] reported in their study of women in Vietnam 16.9% were infected with HPV 16 and/or 18, while others were infected by other high-risk HPV genotypes, including 52, 58, 35 and 45 [22]. In the National Health and Nutrition Examination Survey, Hairi et al., [20] reported the most prevalent high-risk HPV types were 53, 16,

Table 3: Pathology results, HPV prevalence and types.

Characteristic	Southeast Asian women (N=56) n (%)
Cervical cytology results	
Normal	50 (89.3)
ASCUS	2 (3.6)
LGSIL	3 (5.4)
ASCUS r/o HGSIL	0 (0.0)
HGSIL	0 (0.0)
Unsatisfactory	1(1.8)
High-risk HPV infection	
Yes	14 (25.0)
No	42 (75.0)
HPV infection with multiple types	
Yes	6 (10.7)
No	50 (89.3

One woman was missing all pathology and HPV typing results.

Table 4: HPV Genotype Distribution.

HPV genotype	n=14 n (%)
16 (B and/or C)	1 (7.1)
18	0
31	0
33	0
35	2 (14.3)
39	1 (7.1)
45	1 (7.1)
51	4 (28.6)
52	3 (21.4)
56	3 (21.4)
58	1 (7.1)
59	3 (21.4)
68	0
73	2 (14.3)
82	1 (7.1)

51, 52 and 66 for all women [20]. However, their study did not look at Asian Americans separately and only 7% of their population was an ethnicity other than Non-Hispanic white, Non-Hispanic black or Mexican American. Our results along with these other studies suggest that SE Asian women residing in the U.S. may be infected with similar high-risk HPV types seen among SE Asian women residing in their country of origin, regardless of time spent in the United States. Further epidemiologic studies are still needed.

Nearly half of the women in our sample with a HPV infection had concomitant HPV infections with more than one HPV genotype. Trottier et al., [23] found that patients infected with two or more high risk HPV types had an increased risk of abnormal cytology [23]. In a retrospective cohort study of women ages 31-65 years that had HPV typing, Dickson et al., [24] reported infection with multiple HPV types in 12.3% of women [24]. In our study, 10.7% of participants had a HPV infection with 2 or more high-risk HPV types. The impact of concomitant HPV infections on progression to cervical cancer remains unclear. However, a better understanding of the epidemiology of these concomitant infections and the relationship to ethnicity is critical as further HPV vaccination development is underway.

Table 5: HPV Genotypes in participants with concomitant infections.

Participant	HPV 16	HPV 35	HPV 39	HPV 45	HPV 51	HPV 52	HPV 56	HPV 58	HPV 59	HPV 82
1		■					■			
2	■					■				
3		■			■					
4			■			■				
5					■			■	■	
6				■			■			■

In the U.S., to date few HPV vaccination studies have included large numbers of Asian women and most do not differentiate between Asian American subgroups. Specifically, the current vaccination studies have included very few SE Asian women. This is crucial because the cervical cancer incidence between Asian subgroups differs greatly. This is likely multifactorial because SE Asian women are less likely to participate in screening and may be less likely to participate in research studies [13,25,26] Our study is one of the only studies to date in the U.S. that recruited SE Asian women presenting for gynecologic care and performed HPV typing, regardless of cervical cytology results. While our study has inherent limitations due to the small sample size in one geographic location, strength of our study was that we were able to demonstrate that recruitment of SE Asian women is feasible. However, recruitment in our study was slower than anticipated as we excluded women that had any of the HPV vaccine series.

In conclusion, while approximately 70% of cervical cancers in the U.S. and Europe are caused by HPV 16 and 18, only 60% to 70% of cervical cancer are associated with those serotypes in parts of Asia. It appears that there may be differences in HPV genotypes found among SE Asian women residing in the U.S. as well. Recruitment of SE Asian women in cervical cancer prevention studies is feasible. Increased inclusion of SE Asian women in future vaccination studies as well as analysis of results by Asian American subgroups is warranted.

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