Is there any correlation between frequent lower genital Tract Infections and Human Papillomavirus Infection at the commune level?

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Abstract

Objective: *To investigate the association between lower genital tract infection and Human Papillomavirus (HPV) infection.*

Methods: *A descriptive cross-sectional study of 1,007 sexually active women aged 21 to 70 in three areas of Quang Tri province (Hai Lang, Trieu Phong and Gio Linh). The duration of data collection is from July 2019 to July 2020. The cases were evaluated by gynecology to determine the condition of the vaginal discharge and to record normal and abnormal signs and symptoms. Specimens from cervical canal were inspected under a microscope and tested for HPV-DNA using a real-time PCR assay.*

Results: *There were 33 HPV-positive cases, accounting for 3.5% of total cases. Vaginitis caused by bacteria, including bacteria, bacteriophages, and Gardnerella vaginalis, accounted for the largest prevalence of lower genital tract infections at 65.8%, followed by vaginitis caused by Candida fungi at 10.5% and Trichomonas vaginalis at the lowest rate of 0.2%. No statistically significant association was found between HPV infection and vaginitis caused by Bacteria, Gardnerella vaginalis, Candida, and Trichomonas vaginalis, as well as socio-demographic characteristics such as age, education, age at first sexual intercourse, number of sexual partners, marital status, number of children, and smoking (p > 0.05).*

Conclusion: *Despite the fact that lower genital tract infection and HPV infection are not uncommon at the commune level, no association was discovered between the two.*

Keywords: *HPV (Human papilloma virus), lower genital tract infection, commune level.*

1. INTRODUCTION

Cervical cancer is a malignancy disorder of the squamous or glandular epithelium of the cervix that often affects women over the age of 30, ranking second in terms of morbidity and mortality rate among female genital cancers. In which genital high-risk HPV infection is regarded a necessary cause of cervical cancer [1], which is the fourth most prevalent malignancy among women worldwide, affecting around 530 thousand people year [1], [2], [3]. Important determinants in the development of cervical cytopathology [3] include HPV-specific genotypes, viral load, and coinfection with several genotypes. A correlation between cervical dysplasia and HPV infection has been established, although only a tiny percentage of women with HPV acquire cervical cancer, indicating that other cofactors may be involved. And many additional cofactors, such as long-term use of hormonal contraceptives, high parity, smoking, immunosuppression, and specific nutritional deficits, contribute to this cytopathological process [3]. Moreover, it has been documented that sexually transmitted infections interact with HPV as cofactors in the evolution of cervical neoplasias [4]. Chlamydia trachomatis and Trichomonas vaginalis, for example, have been shown to be positively linked with chronic high-risk HPV infection [4, 5]. Vielot et al. [6] also observed that Chlamydia trachomatis was an important risk factor for long-term high-risk HPV infection. Ureaplasma spp. was linked to high-risk HPV infection and aberrant cervical cytopathology, according to a meta-analysis of 22 studies including 16,181 women [7]. However, the aforementioned findings remain inconclusive.

According to clinical findings, an imbalance of the vaginal environment is associated with cervical neoplasia. It is known that bacteria, *Trichomonas spp.*, and *Candida spp. Gardnerella vaginalis*-caused bacterial vaginosis significantly alters the vaginal ecology, mostly as a result of a large number of bacteria displacing the Lactobacillus group normally seen in vaginal discharges. These microbiological modifications are also caused by the Candida fungus, which modifies the synthesis of hydrogen peroxide and lactic acid. It decreases vaginal pH, increases the availability of substrates, and inhibits the limiting impact of Lactobacillus flora [8]. Candidiasis can manifest with symptoms like itching and irritation, as well as inflammatory characteristics. Similar to *Candida, Trichomonas* also generates inflammatory responses, which promote contacts between the sexually transmitted disease-causing parasite and the squamous epithelium, resulting in vascular growth, edema, and erosion. In certain situations, surface layers

and even cell necrosis are seen. This study aimed to investigate the association between lower genital tract infection and Human Papillomavirus (HPV) infection in Quang Tri Province.

2. METHODS

This descriptive cross-sectional study recruited women ages 21 to 65 with a history of sexual activity who agreed to participate after receiving clear information. Between July 2019 and July 2020, a total of 1010 cases were recruited from 12 communes in three districts of Quang Tri province, including Hai Lang, Trieu Phong, and Gio Linh. Women who had a total hysterectomy, became pregnant, or in the postpartum duration, had a vaginal suppository or douching within the previous 24 hours were excluded from the study.

Any discovered precancerous or cancerous lesions will be treated accordingly.

$$n = \frac{Z^2_{\alpha/2} \times p(1-p)}{d^2}$$

The sample size was calculated according to the formula:

- n: sample size for the study
- p: Rate of HPV infection, choose p = 0.0664 according to research by author Lam Duc Tam in 2017 [29].
- d: allowable error between sample rate and population proportion; d = 0.02.
- α: level of statistical significance.
- Z: confidence coefficient (with alpha = 0.05, Z 0.975 = 1.96).

Applying the formula, the sample size is 655 people. To avoid sampling error: we chose design validity of 1.5 times so that the sample size is 655 x 1.5 = 983 people.

All cases will be interviewed for administrative information, undergo a mass gynecological examination, have cervical swab samples collected for DNA extraction, and the real-time PCR RBD technique will be used to detect positive samples; Choose this positive sample for HPV typing using the real-time PCR - reverse dot blot method. Following is an explanation of the results of the patient samples: The cobas HPV test operating on the cobas 4800 system returns four channels for the same test result.

- Channel 1: 12 high-risk types
- Channel 2: Detecting HPV 16
- Channel 3: Detecting HPV 18
- Channel 4: Beta-Globin Internal Control

HPV positive: if positive for any type: type 16, 18 or group 12 high-risk types.

The results are recorded on the data collection form before being entered into the Epi-data software and processed using the SPSS 20 application. Chi-square test analysis of the association between parameters associated to HPV infection condition. When $p < 0.05$, the test is statistically significant.

The Ethics Committee of Hue University of Medicine and Pharmacy evaluated, commented on, and morally and scientifically approved the study in accordance with the regulations.

3. RESULTS

Of 1,200 enrolled women aged 21 to 70 in 12 communes in the province of Quang Tri, 75 cases of lost track and 118 cases relating to sample transportation and handling were removed. In the remaining sample of 1,007 instances, we found the following results:

Table 1. HPV infection status among patients in various age groups

Age groups (years)	HPV (+) n, (%)	HPV (-) n, (%)	Total n, (%)	p
20-29	1 (1.9)	53 (98.1)	54 (100)	
30-39	11 (4.1)	256 (95.9)	267 (100)	
40-49	13 (3.4)	367 (96.6)	380 (100)	< 0.05
50-59	8 (3.1)	254 (96.9)	262 (100)	
60-65	0 (0)	44 (100)	44 (100)	
The mean age $\bar{X} \pm$ SD	42.4 ± 8.4	44.3 ± 9.2		0.25
Total	33 (3.3)	974 (96.7)	1007 (100)	

This difference was not statistically significant ($p > 0.05$): the mean age of the HPV-infected group was 42.4 ± 8.4 and the negative-HPV group was 44.3 ± 4.3.

Nevertheless, the frequency of HPV infection varies by age group ($p < 0.05$): The largest incidence of HPV infection occurs among women aged 30 to 49. (7.5%). No one over 60 years old were infected with HPV (Table 1). The HPV infection rate among 20-29-year-old women is 1.9%, but the rate among 50-59-year-old women is 3.1%.

Table 2. Relationship between the HPV infection and some risk factors

Risk factors	HPV (-) n, (%)	HPV (+) n, (%)	Total n, (%)	p
Education				
Under high school	93 (97.9)	2 (2.1)	95 (100)	0.5
Above high school	881 (96.6)	31 (3.4)	912 (100)	
Age of first sex				
≤ 18 years old	43 (97.7)	1 (2.3)	44 (100)	0.5
> 18 years old	931 (96.7)	32 (3.3)	963 (100)	
Number of sexual partners				
1 person	941 (96.7)	32 (3.3)	973 (100)	0.7
≥ 2 persons	33 (97.1)	1 (2.9)	34 (100)	
Marriage				
Single	4 (100)	0 (0,0)	4 (100)	0.5
Married	952 (97.7)	30 (3.1)	982 (100)	
Divorced, widowed	18 (85.7)	3 (14.3)	21 (100)	
Number of children				
0	6 (100)	0 (0,0)	6 (100)	
1- 2	399 (96.4)	15 (3.6)	414 (100)	0.7
3 - 4	492 (96.7)	17 (3.3)	509 (100)	
≥ 5	77 (98.7)	1 (1.3)	78 (100)	
Smoking				
Non-smoker (both)	546 (96.6)	19 (3.4)	565 (100)	0.6
Passive smoker	419 (96.8)	14 (3.2)	433 (100)	
Active smoker	9 (100)	0 (0,0)	9 (100)	

The results of a statistical analysis of sociodemographic factors and cervical HPV infection status were inconclusive (p > 0.05).

Table 3. HPV type classification

HPV results	Number (n)	Rate (%)
Negative	974	96.7
Positive	33	3.3
- Type 16	6	0.6
- Group of 12 types	26	2.6
- Group of 12 types and type 16	1	0.1
Total	**1007**	**100**

In a survey of 1,007 women between the ages of 21 and 70, we identified 33 HPV-positive cases, accounting for 3.5%, and 96.75% of cases being negative for HPV.

In 33 HPV-positive cases, 6 cases were positive for HPV type 16 (0.6%), 26 cases were positive for group 12 types (2.6%), and 1 case was positive for both types of HPV (type 16 and group 12). (0.1%).

Table 4. Vaginal wet-mount examination results

Vaginal characteristics	Number (n)	Rate (%)
Normal	408	40.4
Bacterial		
- Bacteria vaginitis	547	54.1
- *Gardnerella vaginalis*	117	11.7
Candida spp vaginalis	106	10.5
Trichomonas vaginalis	2	0.2
Atrophy	178	17.6

Among the pathogens in the study group, bacterial vaginosis and bacteria vaginitis accounted for the highest rate at 65.8%. Vaginal atrophy and Candida accounted for 17.6% and 10.5%, respectively, vaginitis caused by Trichomonas vaginalis accounted for the lowest rate of 0.2%.

Table 5. Correlation between Lower Genital Tract and HPV Infection

Vaginal characteristics		HPV (+) n (%)	HPV (-) n (%)	Total (n=1007)	OR (95%CI)	p
Bacteria	Positive	20 (3.6)	527 (96.4)	547	1.31 (0.66 - 2.90)	0.39
	Negative	46 (10)	414 (90)	460		
Gardnerella	Positive	7 (5.9)	111 (94.1)	118	2.09 (0.92 - 5.17)	0.07
	Negative	26 (2.9)	863 (97.1)	889		
Candida spp	Positive	5 (4.7)	101 (95.3)	106	1.54 (0.61 - 4.27)	0.33
	Negative	28 (3.1)	873 (96.9)	905		
Trichomonas vaginalis	Positive	0 (0)	2 (100)	2	-	0.79
	Negative	33 (3.3)	972 (96.7)	1005		
Atrophy	Positive	3 (1.6)	175 (98.4)	178	0.46 (0.14 - 1.58)	0.22
	Negative	30 (3.6)	799 (96.4)	828		

There was no statistically significant correlation between HPV infection and the several types of vaginitis: bacteria, Gardnerella vaginalis, Candida, Trichomonas vaginalis, and atrophy ($p > 0.05$).

4. DISCUSSION

The prevalence of HPV infection in the community was 3.3% in this study. Compared to the outcomes of several domestic and international studies, our result is quite low. The prevalence of HPV infection is higher in studies conducted in Hanoi and Ho Chi Minh City than in our study [9], [10], [11], and [12]. The results of our study are significantly lower than those of studies on the prevalence of HPV among Africans (24%), Germans (28.1%), and Brazilians (14.7%). In other studies, women living in urban have more access to health care services and complicated lifestyle than women living in rural and remote places. Consequently, the rate of HPV infection detection is likewise higher in the urban core.

HPV types 16 and 18 are the most prevalent high-risk HPV types that cause precancerous lesions and cervical cancer. Current diagnostics and screening techniques concentrate on identifying individuals at high risk. In our study, which differs from those of other authors [11], [16], 2.6% of women were infected with high-risk HPV group 12, representing the highest infection rate. The rate of HPV type 16 infection among women was 0.6%, and there was only one case of co-infection with type 16 and group 12. This is also reasonable given that the distribution of HPV types in community populations is highly variable and dependent on the incidence of cytological abnormalities.

Regarding the significance of vaginal co-infections and sexually transmitted diseases in relation to risk factors for developing cervical cancer in relation to these pathogens that are connected with HPV infection, there are contradictory evidence. Among 460 women of childbearing age in A Luoi district, Thua Thien Hue, the rate of genital infections is low, at 37.6%, in Cao Ngoc Thanh's study in 2017. Pathogens include Bacteria (32.4%), Gardnerella vaginosis (35.3%), Candida

(17.3%), both Bacteria and Candida (7.5%), pyogenic bacteria (7.5%), and no case of Trichomonas vaginalis infection [17]. According to research conducted by Nguyen Thi Kim Loan and colleagues in 2019 at Thong Nhat General Hospital in Dong Nai province on more than 380 women of reproductive age, the rate of lower genital tract infections was 72.4%; bacteria was the most prevalent cause, accounting for 65.5%, followed by Candida fungus (29.8%) and Trichomonas vaginalis infection (4.7%) [18].

According to a 2019 study conducted in China on 826 women of reproductive age by Panpan Lv et al., there is a connection between lower genital tract infection and HPV infection. Except for *Candida albicans, Chlamydia trachomatis, U. Urealyticum, Ureaplasma parvum, Trichomonas vaginalis, and Bacterial vaginosis,* the prevalence of infection was higher in HPV-positive women than in HPV-negative women. Multivariate regression analysis revealed that all of these substances are HPV infection risk factors [20]. They explained that persistent inflammation of the lower genital tract can promote the colonization of other bacteria, which act as cofactors in the pathogenesis of cervical lesions that supply and generate chromosomal alterations that can lead to squamous cell carcinoma.

In our investigation, however, we found no statistically significant association between HPV infection and several types of vaginitis, including those caused by bacteria, Gardnerella vaginalis, Candida, Trichomonas vaginalis, and atrophy ($p > 0.05$). This conclusion is comparable to the study conducted by Suelen Paesi and colleagues in 2012 [19]. This is likely due to the fact that changes in pH and modest physiological changes are likely insufficient to alter chronic HPV infection in the lower vaginal tract. Due to the wide variety of pathogens, such as viruses, bacteria, flagellates, and yeasts, the immune system can respond differently to each infection. In addition, this study showed no relationship between HPV and sociodemographic factors or other microbes residing in the female lower vaginal tract. All women with abnormal cytology tests are susceptible to HPV and other vaginal diseases.

In conclusion, despite the fact that lower genital tract infection and HPV infection are not uncommon at the commune level, no association was discovered between the two.

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