Biomedical Science Letters 2022, 28(4): 229~236
https://doi.org/10.15616/BSL.2022.28.4.229
eISSN : 2288-7415

Original Article

Analysis of HR-HPV Prevalence among Unvaccinated Busan Women

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To prevent cervical cancer, human papillomavirus (HPV) bivalent and quadrivalent vaccinations are common, but there is a need for a vaccination system based on the high-risk human papillomavirus (HR-HPV) genotype that differs by region. This study aimed to investigate the prevalence of HPV and the distribution of HR-HPV genotypes in 2,014 women who were not vaccinated against HPV. In this study, HPV DNA testing was performed on 2,014 women not vaccinated against HPV and who visited the Busan Obstetrics and Gynecology Department from September 2020 to July 2021. In addition, liquid-based cytology (LBC) test was performed on 493 cases of HR- HPV genotype infection confirmed by HPV DNA test. The prevalence of HPV among women in Busan was positive in 609 (30.2%) out of 2,014 cases. Among the 609 HPV-positive cases, HR-HPV infection accounted for 493 cases (81.0%), which is a high proportion. Of the total 493 HR-HPV infection cases, liquid-based cytology (LBC) was within normal limits (WNL) in 266 cases (54.0%), atypical squamous cells of undetermined significance (ASCUS) in 97 cases (19.7%), low-grade squamous intraepithelial lesion (LGSIL) in 88 cases (17.8%), and high-grade squamous intraepithelial lesion (HGSIL) in 42 cases (8.5%). Single HR-HPV 52 and 16 accounted for the highest and second highest infection rates, respectively. The high infection rate among women aged 18~39 underscores the need for continuous monitoring. In addition, when there were abnormal findings in the cervical epithelium, HPV 52 was the most common, while in the case of HGSIL, HPV 16 was the most common. The HR-HPV genotypes related to cervical cancer should be continuously collected and monitored for use in health policies, including local and national vaccinations.

Key Words: Human papillomavirus, Cervical cancer, HPV DNA test

INTRODUCTION

Cervical cancer, caused by human papillomavirus (HPV) infection, is the third most common cancer among women worldwide (Muñoz et al., 2003), Notably, the incidence of cervical cancer in Korea is declining (Hong et al., 2021). But given that the rates of HPV infection and cervical cancer among young women in their 20s and 30s are increasing, these topics merit special attention (Sabol et al., 2017; Aro et al., 2019; Hong et al., 2021).

HPV is a highly contagious pathogen that infects the skin or genital mucosa and causes genital warts, precancerous lesions, and cervical cancer (Krashias et al., 2017). High risk (HR)-HPV genotypes have high carcinogenicity that transforms infected cells into cancer, with HPV 16 and 18 as

Received: October 19, 2022 / Revised: November 8, 2022 / Accepted: November 9, 2022
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the representative high-risk groups, for which prophylactic vaccines are being commercialized (Martins et al., 2016; Ma et al., 2019). In addition to HPV types 16 and 18, HPV-31, 33, 34, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68 and 70 have been classified as high-risk genotypes (Burd, 2003).

The distribution of HPV genotypes has been reported to vary between regions and countries (de Sanjosé et al., 2007). Although the infection rates of HPV 16 and 18 are high in South America and Europe, it has been reported that the infection rates of HPV 16 and 18 genotypes are relatively low in cervical cancer patients in East Asia In Korea, the infection rates of HPV 52 and 58 are higher in women in their 30s and 40s than HPV 16 and 18 (Park et al., 2019). To fundamentally prevent cervical cancer, it is necessary to establish a medical health policy that entails inoculating a customized vaccine by identifying the HPV genotype prevalent in each region and country.

For HPV vaccines worldwide, Cervarix's (GlaxoSmith-Kline Biologicals, Brentford, UK) bivalent and Gardasil's (Merck Sharp & Dohme Co., Kenilworth, NJ, USA) quadrivalent vaccines are mainly used; in Korea, free inoculation of these two vaccines is included in the national screening system (Kim et al., 2018). Recently, it was expected that HR-HPV 31, 33, 45, 52, and 58 genotypes would be added due to Gardasil's 9-valent vaccine development (Printz, 2015; Topazian et al., 2018), which would enhance the preventive power (Paz-Zulueta et al., 2018; Kind et al., 2020). The HPV 9-valent vaccine is reportedly more effective in reducing high-grade lesions in the cervix than the 4-valent vaccine (Paz-Zulueta et al., 2018). However, the vaccination rate is not high due to the high vaccine cost that individuals must bear. According to research, there is a cross-protection ability against different HPV genotypes, but the results of studies on the cross-protection ability of vaccines remain insufficient (Malagón et al., 2012; Min et al., 2016). Therefore, if a continuous analysis of HPV prevalence and genotype according to region and country is conducted, vaccine development and vaccination systems suitable for various situations can be established as needed.

This study attempted to secure basic data for cervical cancer prevention by analyzing the HPV prevalence and HR-HPV genotype distribution in women who were not vaccinated with HPV in Busan, Korea.

MATERIALS AND METHODS

Study subjects

In this study, HPV DNA testing was performed on 2,014 women not vaccinated against HPV and who visited the Busan Obstetrics and Gynecology Department from September 2020 to July 2021. The age of the subjects ranged from 20 to 82 years, with an average age of 39.5 years. In addition, liquid-based cytology (LBC) test was performed on 493 cases of HR-HPV genotype infection confirmed by HPV DNA test. Cytological results were diagnosed by a pathologist and classified according to The Bethesda System (TBS). The TBS classification system classified within normal limits (WNL), atypical squamous cells of undetermined significance (ASCUS), low-grade squamous intraepithelial lesion (LGSIL), high-grade squamous intraepithelial lesion (HGSIL), and squamous cell carcinoma (SCC). This study was conducted after obtaining approval from the Bioethics Committee of the Catholic University of Busan (CUPIRB 2020-01-011).

HPV DNA detection

Cervical decidual epithelial cells were collected, and DNA was extracted using a QIAamp DNA kit (QIAGEN Inc., Chatsworth, CA, USA). First, 20 μL proteinase K was added to a 1.5 mL e-tube with a 200 μL sample. Next, 200 μL buffer AL was added, mixed for 15s, and incubated for 10 min. Then, 200 μL ethanol (96~100%) was added to the sample and mixed for 15s. Thereafter, the mixture was transferred to a 2 mL collection tube and centrifuged at 6,000 x g for 1 min. Through the washing step, pure DNA was extracted.

HPV genotyping was performed by liquid bead microarray (LBMA) using the Omniplex-HPV kit (geneMatrix Inc., Seongnam, South Korea) according to the manufacturer's instructions. Omniplex-HPV kit is a kit that can detect a total of 40 types of HPV; 19 types in the high-risk group (HPV-16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 69, 73, 82) and 21 types in the low-risk group (HPV-6, 11, 30, 32, 40, 42, 43, 44, 54, 55, 61, 62, 67, 70,

71, 72, 74, 81, 83, 84, 87). For single-closed tube nested PCR, a total of 25 μL of reaction solution was used by mixing 20 μL of Mastermic mixture and 5 μL of extracted DNA. For PCR amplification, using a thermal cycler (Bio-Rad Lab., Hercules, Ca, USA) at 50℃ for 2 min and at 95℃ for 15 min, after two denaturation steps, 95℃ for 30 sec, 55℃ for 30 sec and 72℃ for 60 sec, after the pre-amplification process by performing the second reaction cycle 10 times, the reaction cycle was performed 50 times at 95℃ for 30 sec, 40℃ for 60 sec and 70℃ for 30 sec to amplify and react at 72℃ for 10 min. For the hybridization reaction, 45 μL of the solution mixture I kit provided by the manufacturer was dispensed, 5 μL of the PCR product was added, reacted at 95℃ for 5 min and 53℃ for 1 h, and then the supernatant was removed. Next, 90 μL of Solution mixture II was dispensed and reacted at 53℃ for 5 min, and then the supernatant was removed. Finally, 80 μL of OPV-Buffer 3 solution was added, and the mean fluorescence intensity (MFI) values of 40 HPV genotypes were checked using the MAGPIX® system (Luminex Corp., Austin, TX, USA). Results were interpreted as HPV genotype positive when the MFI value was 100 or higher.

Liquid based cytology (LBC) test

The cervical decidual epithelial cells of the women were collected and placed in a cell prep vial, a liquid cytometry container, and fixed for more than 30 min. Afterward, the cell prep vial where the cell fixation was completed was attached (Biodyne, Seoul, South Korea), and a suction tube in the vial was used to aggregate the cells by attaching the slide to the blowing membrane. A uniform sample slide was prepared as a monolayer without overlapping between cells. After fixing the prepared slides in 95% ethyl alcohol for 30 min, Pap staining was performed in automatic staining equipment (Autostainer XL, Leica, Wetzlar, Germany). After staining with hematoxylin for 2 min, it was washed with water, decolorized with 0.5% HCL, washed with water, and then stained with OG-6 and EA-50 solutions for 1 min each. The slides were manufactured through dehydration, clearing, and mounting processes.

RESULTS

HPV prevalence and single HR-HPV genotype distribution in 2,014 female patients

The prevalence of HPV among women in Busan was positive in 609 cases (30.2%) and negative in 1,405 cases (69.8%) out of 2,014 cases. For the distribution of HPV infection genotypes, out of 609 cases, single LR-HPV was positive in 102 cases (16.7%), single HR-HPV was positive

Table 1. HPV prevalence and single HR-HPV genotype distribution in 2,014 female patients

Infection	Cases N=2,014 (%)
HPV Negative	1,405 (69.8)
HPV Positive	609 (30.2)
Single LR-HPV	102 (16.7)
Multiple HPV	237 (38.9)
LR + LR	14 (5.9)
LR + HR	138 (58.2)
HR + HR	85 (35.9)
Single HR-HPV	270 (44.3)
HPV-16	33 (12.2)
HPV-18	11 (4.1)
HPV-26	2 (0.7)
HPV-31	9 (3.3)
HPV-33	4 (1.5)
HPV-35	6 (2.2)
HPV-39	21 (7.8)
HPV-45	6 (2.2)
HPV-51	21 (7.8)
HPV-52	57 (21.1)
HPV-53	20 (7.4)
HPV-56	13 (4.8)
HPV-58	15 (5.6)
HPV-59	4 (1.5)
HPV-66	16 (5.9)
HPV-67	1 (0.4)
HPV-68	5 (1.9)
HPV-70	23 (8.5)
HPV-73	1 (0.4)
HPV-82	2 (0.7)

Table 2. Analysis of cytological results according to 493 HR-HPV genotypes

Infection	Cytological results				
	Cases	Normal	ASCUS	LGSIL	HGSIL
	N=493	N=266	N=97	N=88	N=42
Single HR-HPV	270	145	54	41	30
HPV-16	33	16	4	1	12
HPV-18	11	5	1	1	4
HPV-26	2	2	−	−	−
HPV-31	9	3	2	1	3
HPV-33	4	−	3	1	−
HPV-35	6	1	5	−	−
HPV-39	21	16	1	4	−
HPV-45	6	4	2	−	−
HPV-51	21	10	6	4	1
HPV-52	57	30	11	10	6
HPV-53	20	13	4	3	−
HPV-56	13	1	3	8	1
HPV-58	15	7	3	3	2
HPV-59	4	3	1	−	−
HPV-66	16	12	1	3	−
HPV-67	1	1	−	−	−
HPV-68	5	4	−	−	1
HPV-70	23	16	6	1	−
HPV-73	1	−	1	−	−
HPV-82	2	1	−	1	−
Multiple HR-HPV					
LR + HR	138	75	30	28	5
HR + HR	85	46	13	19	7

in 270 cases (44.3%), and multiple HPV was positive in 237 cases (38.9%). For the distribution of multiple HPV infections, LR + LR multiple HPV infections accounted for 5.9% (14/237), LR + HR multiple HPV infections for 58.2% (138 /237), and HR + HR multiple HPV infections for 35.9% (85/270) (Table 1). This means that out of 609 HPV-positive cases, HR-HPV infection accounted for 493 (81.0%), which is a high proportion.

For the genotypes of single HPV infections, HPV 52 was the most common with 21.1% (57/270), followed by HPV 16 with 12.2% (33/270). In addition, HPV 70 accounted for 8.5% (23/270), HPV 51 and 39 for 7.8% (21/270), and HPV 53 for 7.4% (20/270).

Analysis of cytological results according to 493 HR-HPV infection

LBC results were analyzed for 493 cases positive for HR-HPV infection. Of the 493 HR-HPV infection cases, LBC was WNL in 266 cases (54.0%), ASCUS in 97 cases (19.7%), LGSIL in 88 cases (17.8%), and HGSIL in 42 cases (8.5%) (Table 2).

Out of 266 cases diagnosed as WNL in LBC, single HR-HPV infection was found in 145 cases (54.5%), LR + HR multiple HPV infections in 75 cases (28.2%), and HR + HR multiple HPV infections in 46 cases (17.3%). Out of 97 cases diagnosed as ASCUS in LBC, single HR-HPV infection was found in 54 cases (55.7%), LR + HR multiple

Table 3. Analysis of the prevalence of seven types of HR-HPV according to age distribution

Age	Cases	HR-HPV						
		16	18	31	33	45	52	58
20~29	68	14	5	10	−	5	23	11
30~39	108	14	16	13	3	2	42	18
40~49	60	15	4	7	2	3	22	7
50~59	46	12	2	3	2	2	19	6
60~69	22	6	1	3	2	−	8	2
≥70	6	2	−	1	2	−	−	1
Total	310	63	28	37	11	12	114	45

HPV infections in 30 cases (30.9%), and HR + HR multiple HPV infections in 13 cases (13.4%). Out of 88 cases diagnosed as LGSIL in LBC, single HR-HPV infection was found in 41 cases (46.6%), LR + HR multiple HPV infections in 28 cases (31.8%), and HR + HR multiple HPV infections in 19 cases (21.6%). Out of 42 cases diagnosed as HGSIL in LBC, single HR-HPV infection was found in 30 cases (71.4%), LR + HR multiple HPV infections in five cases (11.9%), and HR + HR multiple HPV infections in seven cases (16.7%).

For the distribution of single HR-HPV genotypes in cases of cervical intraepithelial abnormality (ASCUS + LGSIL + HGSIL) in LBC, HPV 52 was the most common with 21.6% (27/125), followed by HPV 16 with 13.6% (17/125) and HPV 56 with 9.6% (12/125). For the distribution of single HR-HPV genotypes in the case of HGSIL in LBC, HPV 16 was the highest with 40.0% (12/30), followed by HPV 52 with 20.0% (6/30), and HPV 18 with 13.3% (4/30).

Analysis of the prevalence of seven types of HR-HPV according to age distribution

Table 3 examines the age distribution of seven-valent HR-HPV genotypes among single and multiple HR-HPV infections. As can be seen, 108 cases (34.8%) between the ages of 30 and 39 accounted for the highest number out of 310 cases, followed by 68 cases (21.9%) among those aged 20~29, 60 cases (19.4%) among those aged 40~49, 46 cases (14.8%) among those aged 50~59, 22 cases (7.1%) among those aged 60~69, and six cases (1.9%) among those over 70 years.

Examining the seven types of HR-HPV genotypes according to age distribution, out of 310 cases, HPV 52 was the most common with 114 cases (36.8%), followed by HPV 16 with 63 cases (20.3%), HPV 58 with 45 cases (14.5%), HPV 31 with 37 cases (11.9%), HPV 18 with 28 cases (9.0%), HPV 45 with 12 cases (3.9%), and HPV 11 with 33 cases (3.5%).

DISCUSSION

In Korea, HPV is known as the main cause of cervical cancer, so HPV vaccination is administered as a national mandatory free vaccination for women under the age of 12 (Kim et al., 2018). In addition, policy efforts are being exerted to actively prevent cervical cancer by lowering the national screening age for cervical cytology, which was previously conducted for those aged 20 to 30 years (Won et al., 2020). Although the mortality rate due to cervical cancer has significantly declined due to these efforts (Tran et al., 2020), the prevalence of HPV is still reportedly high among young women (Sabol et al., 2017; Aro et al., 2019; Hong et al., 2021), Therefore, research for monitoring the potential risk of cervical cancer due to HR-HPV is steadily increasing. A meta-analysis with data from 65 studies from 14 high-income countries published in 2019 found that 5~8 years after HPV vaccination, the prevalence of HR-HPV decreased by 83% for women 13~19 years old and 66% for women 20~24 years old. In addition, among women who were screened for cervical cancer 5 to 9 years after vaccination, CIN2+ was significantly reduced by 51% at the age of

15~19 and by 31% at the age of 20~24 (Drolet et al., 2019). In this study, the overall prevalence of HPV among women not vaccinated against HPV was 30.2% (609/2,014), and the prevalence of HR-HPV reached as high as 81.0% (493/609).

Although it has been reported that HPV genotypes differ between regions and countries (de Sanjosé et al., 2007), the prevalence of HPV 16 and 18 are the highest among women worldwide (Clifford et al., 2005). Therefore, in Korea, bivalent and quadrivalent vaccines including HPV 16 and 18 are designated as mandatory national vaccinations. However, since it has been reported that the frequencies of infection with HPV 52 and 58 are high in Asia (de Sanjosé et al., 2007; Long et al., 2018), selecting vaccines for national vaccination has elicited interest. In this study, the single HR-HPV infection rate was 21.1% (57/270) for HPV 52, higher than 12.2% (33/270) for HPV 16 (Table 1). In the analysis of the HR-HPV infection rate according to age, HPV 52 accounted for 36.8% (114/310), which was higher than that of HPV 16, which was 20.3% (63/310). Recently, 9-valent vaccines, including HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58, have been released, thus expanding the range of prevention. They have been reported to be particularly effective in preventing HPV in adult women (Printz, 2015; Topazian et al., 2018). In another study, five HPV genotypes not included in the quadrivalent vaccine were significantly associated with high-grade lesions in the cervix, except for HPV 16 and 18, which explains the positive effect of 9-valent vaccination (Paz-Zulueta et al., 2018). Therefore, the adoption of a 9-valent vaccine containing HPV 52 as a vaccine for mandatory national vaccinations should be considered.

The cumulative infection rate of HPV reaches about 50% within several years of starting sexual activity (Castle, 2004), and it is reported that the prevalence of HPV decreases with increasing age (Walboomers et al., 1999; Hong et al., 2021). This is interpreted as a high prevalence of HPV in sexually active young women, and monitoring for HR-HPV infection is the most effective way to prevent cervical cancer. In this study, the HR-HPV infection rate for women aged 20 to 39 was high at 56.8% (176/310). In particular, HPV 52 accounted for 36.9% (65/176), HPV 58 for 16.5% (29/176), and HPV 16 for 15.9% (28/176), underscoring that these are high-risk genotypes that require follow-up.

Most cases of HPV infection are asymptomatic and are known to be cured naturally through an immune response within a few years (Cubie, 2013). However, since the natural antibody response to HPV is slow and the antibody titer is low (WHO, 2014), it has been suggested that if HR-HPV infection persists, it may be a factor in the development of cervical neoplasia (Myers et al., 2000). Not all HPV infections cause cervical cancer, so the analysis and follow-up of HR-HPV infection, which are related to the development of intracervical tumors, are more important. HPV 16 should be allocated particular attention because it reportedly has the highest infection rate in cervical cancer (Sasagawa et al., 2001). In this study, 227 cases (46.0%) showed intraepithelial abnormalities among 493 HR-HPV cases. In the single HR-HPV infection rate, HPV 52 accounted for the highest infection rate, while in HGSIL, single HPV 16 was the highest at 40% (12/30), indicating their association with cancer.

In conclusion, the prevalence of HPV among women in Busan, Korea who did not receive HPV vaccine was 30.2% (609/2,014), and the HR-HPV infection rate was as high as 81.0% (493/609). Single HR-HPV type 52 and type 16 showed the highest infection rate in that order, and the high infection rate among young women aged 18~39 suggests the need for continuous monitoring. In addition, in the cytological results, when there were abnormal findings of cervical epithelium, HPV type 52 was the most common, and when there were high-grade intraepithelial abnormalities, HPV type 16 was more common. It is thought that the HR-HPV genotypes related to cervical cancer should be continuously collected and followed for use in health policies, including local and national vaccination.

ACKNOWLEDGEMENT

This research was funded by the National Research Foundation of Korea. The grant was funded by the Korean Government, grant number NRF-2020R1A2C1102228.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

Aro K, Nieminen P, Louvanto K, Jakobsson M, Virtanen S, Lehtinen M, Dillner J, Kalliala I. Age-specific hpv type distribution in high-grade cervical disease in screened and unvaccinated women. Gynecol Oncol. 2019. 154: 354-359.

Burd EM. Human papillomavirus and cervical cancer. Clin Microbiol Rev. 2003. 16: 1-17.

Castle PE. Beyond human papillomavirus: The cervix, exogenous secondary factors, and the development of cervical precancer and cancer. J Low Genit Tract Dis. 2004. 8: 224-230.

Clifford GM, Gallus S, Herrero R, Muñoz N, Snijders PJ, Vaccarella S, Anh PT, Ferreccio C, Hieu NT, Matos E, Molano M, Rajkumar R, Ronco G, de Sanjosé S, Shin HR, Sukvirach S, Thomas JO, Tunsakul S, Meijer CJ, Franceschi S. Worldwide distribution of human papillomavirus types in cytologically normal women in the international agency for research on cancer hpv prevalence surveys: A pooled analysis. Lancet. 2005. 366: 991-998.

Cubie HA. Diseases associated with human papillomavirus infection. Virology. 2013. 445: 21-34.

de Sanjosé S, Diaz M, Castellsagué X, Clifford G, Bruni L, Muñoz N, Bosch FX. Worldwide prevalence and genotype distribution of cervical human papillomavirus DNA in women with normal cytology: A meta-analysis. Lancet Infect Dis. 2007. 7: 453-459.

Drolet M, Bénard É, Pérez N, Brisson M, Ali H, Boily MC, Baldo V, Brassard P, Brotherton JML, Callander D, Checchi M, Chow EPF, Cocchio S, Dalianis T, Deeks SL, Dehlendorff C, Donovan B, Fairley CK, Flagg EW, Gargano JW, et al. Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: Updated systematic review and meta-analysis. The Lancet. 2019. 394: 497-509.

Hong S, Won YJ, Lee JJ, Jung KW, Kong HJ, Im JS, Seo HG. Cancer statistics in korea: Incidence, mortality, survival, and prevalence in 2018. Cancer Res Treat. 2021. 53: 301-315.

Kim MA, Han GH, Kim JH, Seo K. Current status of human papillomavirus infection and introduction of vaccination to the national immunization program in korea: An overview. J Korean Med Sci. 2018. 33: e331.

Kind AB, Pavelyev A, Kothari S, El Mouaddin N, Schmidt A, Morais E, Guggisberg P, Lienert F. Assessing the epidemiological impact on cervical cancer of switching from 4-valent to 9-valent hpv vaccine within a gender-neutral vaccination programme in switzerland. BMC Public Health. 2020. 20: 671.

Krashias G, Koptides D, Christodoulou C. Hpv prevalence and type distribution in cypriot women with cervical cytological abnormalities. BMC Infect Dis. 2017. 17: 346.

Long W, Yang Z, Li X, Chen M, Liu J, Zhang Y, Sun X. Hpv-16, hpv-58, and hpv-33 are the most carcinogenic hpv genotypes in southwestern china and their viral loads are associated with severity of premalignant lesions in the cervix. Virol J. 2018. 15: 94.

Ma DM, Sun MX, Li XY, Li S, Nie XJ, Jin DH, Chen LM. Distribution of high-risk human papillomavirus genotypes in male attendees at a clinic for sexually transmitted infections in northern china. Eur Rev Med Pharmacol Sci. 2019. 23: 9714-9720.

Malagón T, Drolet M, Boily MC, Franco EL, Jit M, Brisson J, Brisson M. Cross-protective efficacy of two human papillomavirus vaccines: A systematic review and meta-analysis. Lancet Infect Dis. 2012. 12: 781-789.

Martins TR, Mendes de Oliveira C, Rosa LR, de Campos Centrone C, Rodrigues CL, Villa LL, Levi JE. Hpv genotype distribution in brazilian women with and without cervical lesions: Correlation to cytological data. Virol J. 2016. 13: 138.

Min KJ, Kwon SH, Kim S, Kim HJ, Seong SJ, Song YJ, Shin JW, Lee KH, Lim MC, Chung HH, Ju W, Hong JH, Lee JW, Kim JW, Bae DS, Lee JK. Preventive vaccination against cervical cancer: Korean society of gynecologic oncology guideline. J Gynecol Oncol. 2016. 27: e30.

Muñoz N, Bosch FX, de Sanjosé S, Herrero R, Castellsagué X, Shah KV, Snijders PJ, Meijer CJ. Epidemiologic classification of human papillomavirus types associated with cervical cancer. N Engl J Med. 2003. 348: 518-527.

Myers ER, McCrory DC, Nanda K, Bastian L, Matchar DB. Mathematical model for the natural history of human papillomavirus infection and cervical carcinogenesis. Am J Epidemiol. 2000. 151: 1158-1171.

Park E, Kim JY, Choi S, Kim DS, Oh YL. Carcinogenic risk of human papillomavirus (hpv) genotypes and potential effects of hpv vaccines in korea. Sci Rep. 2019. 9: 12556.

Paz-Zulueta M, Álvarez-Paredes L, Rodríguez Díaz JC, Parás-Bravo P, Andrada Becerra ME, Rodríguez Ingelmo JM, Ruiz García MM, Portilla J, Santibañez M. Prevalence of high-risk hpv genotypes, categorised by their quadrivalent and nine-

valent hpv vaccination coverage, and the genotype association with high-grade lesions. BMC Cancer. 2018. 18: 112.

Printz C. Fda approves gardasil 9 for more types of hpv. Cancer. 2015. 121: 1156-1157.

Sabol I, Milutin Gašperov N, Matovina M, Božinović K, Grubišić G, Fistonić I, Belci D, Alemany L, Džebro S, Dominis M, Šekerija M, Tous S, de Sanjosé S, Grce M. Cervical hpv type-specific pre-vaccination prevalence and age distribution in croatia. PLoS One. 2017. 12: e0180480.

Sasagawa T, Basha W, Yamazaki H, Inoue M. High-risk and multiple human papillomavirus infections associated with cervical abnormalities in japanese women. Cancer Epidemiol Biomarkers Prev. 2001. 10: 45-52.

Topazian HM, Kundu D, Peebles K, Ramos S, Morgan K, Kim CJ, Richter KL, Brewer NT, Peris M, Smith JS. Hpv vaccination recommendation practices among adolescent health care providers in 5 countries. J Pediatr Adolesc Gynecol. 2018. 31: 575-582.e572.

Tran KN, Park Y, Kim BW, Oh JK, Ki M. Incidence and mortality of cervical cancer in vietnam and korea (1999-2017). Epidemiol Health. 2020. 42: e2020075.

Walboomers JM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, Snijders PJ, Peto J, Meijer CJ, Munoz N. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. J Pathol. 1999. 189: 12-19.

WHO. Human papillomavirus vaccines: Who position paper, october 2014. Wkly Epidemiol Rec. 2014. 89: 465-491.

Won S, Kim MK, Seong SJ. Clinical management of abnormal pap tests: Differences between us and korean guidelines. J Pathol Transl Med. 2020. 54: 213-219.

https://doi.org/10.15616/BSL.2022.28.4.229

Cite this article as: Kim DH, Lee KE. Analysis of HR-HPV Prevalence among Unvaccinated Busan Women. Biomedical Science Letters. 2022. 28: 229-236.