Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Obstetrics & Gynecology

HPV-DNA Genotype Positivity and its Relationship with Gynecological Symptoms

Sabera Khatun[1], Syeda Ummay Kulsum[2*], Anwarul Karim[3]

[1]Professor (Founder & Ex-Chairman) Department of Gynecological Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh
[2]Assistant Professor, Department of Obstetrics & Gynecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh
[3]Medical Officer, Green Life Medical College, Dhaka, Bangladesh

DOI: 10.36347/sjams.2021.v09i06.004 | **Received:** 11.04.2021 | **Accepted:** 22.05.2021 | **Published:** 03.06.2021

***Corresponding author:** Syeda Ummay Kulsum
Assistant Professor, Department of Obstetrics & Gynecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh

Abstract **Original Research Article**

Background: Human papillomavirus is a necessary but not sufficient cause of cervical cancer all around the world. Vaccination is considered the primary way to prevent cervical cancer. Bangladesh government has been providing a bivalent HPV vaccine containing HPV 16 and 18 for girls aged 10 years old routinely since this year. This study was to observe the predominant serotypes of the HPV virus among Bangladeshi women. ***Aim of the study:*** This study was undertaken to identify the most prevalent HPV genotypes in a cohort of patients presenting with gynecological complaints and to evaluate the relationship between HPV-DNA Genotype positivity and associated clinical features. ***Methods:*** This was a Descriptive type of Observational Quantitative study. The study was conducted at the Central Hospital, Dhaka, Bangladesh, between Jan 2017 and Jan 2021. During the study period a total of 244 patients were enrolled and analyzed in this study. The data was collected from the prescriptions and reports of the patients who came to the chamber of a renowned gynecologist. The physicians and statisticians analyzed the qualitative and quantitative data. ***Results:*** Among the 244 samples collected, 38 patients were positive for HPV genotype; 18(7.44%) of them were genotype 16, 5(2.07%) had genotype 52, 3(1.24%) had genotype 68, 3(1.24% had genotype 51, 2(0.83%) women had 56, 2(0.83%) had genotype 18, 1 each had genotype 39, 45 and 66. Regular cervical cancer screening is strongly recommended even if the women have been vaccinated against HPV, as our vaccine 'Cervarix1' will not cover all the genotypes of the HPV found in the cervical sample of the women of our country. ***Conclusion:*** HPV infection, the leading cause of cervical cancer, is preventable through vaccination and early detection by screening. This study highlights the need for large-scale research to identify prevalent genotypes in Bangladesh, aiding vaccine selection. Strengthening awareness, vaccination, and regular screening can significantly reduce cervical cancer cases among Bangladeshi women.

Keywords: Human Papillomavirus (HPV) Genotype, Cervical Cancer, and Gynaecological Symptoms.

INTRODUCTION

Human Papilloma Virus (HPV) is a well-established necessary, though not solely sufficient, etiological agent for the development of cervical cancer. It represents a significant global health concern, particularly in low- and middle-income countries where cervical cancer remains a leading cause of cancer-related morbidity and mortality among women. Cervical cancer affects approximately 604,127 new cases annually, with 88% occurring in low- and middle-income countries. It leads to an estimated 341,831 deaths each year, primarily in developing nations [1]. In Bangladesh, cervical cancer is the second most common cancer among women and accounts for the highest number of cancer-related deaths. In the year 2018, 8068 new cases of cervical cancer and 5214 deaths were reported in Bangladesh [2]. Persistent infection with high-risk HPV genotypes is responsible for nearly 95% of cervical cancer cases worldwide [3]. The virus infects epithelial tissues, particularly the transformation zone of the cervix, where oncogenic types can integrate into host DNA and drive cellular transformation. While over 200 genotypes of HPV have been identified [4], approximately 13 high-risk types are

associated with carcinogenesis, with HPV types 16 and 18 alone accounting for nearly 70% of cervical cancer cases [5]. Prophylactic vaccination has emerged as the most effective strategy for primary prevention. The World Health Organization (WHO) recommends HPV vaccination for girls aged 9–14 years before the onset of sexual activity to achieve maximum protective efficacy [6]. In addition, cervical cancer screening starting from age 30 (or 25 for women living with HIV) is crucial for early detection and treatment of precancerous lesions, significantly reducing cancer incidence and mortality [7]. Bangladesh has introduced the HPV bivalent vaccine Cervarix®, which targets HPV types 16 and 18 [8]. While this is a promising public health advancement, limited data exist regarding the circulating HPV genotypes in the Bangladeshi population and how these correlates with clinical symptoms and other risk factors. Therefore, this study was undertaken to identify the most prevalent HPV genotypes in a cohort of patients presenting with gynecological complaints and to evaluate the relationship between HPV-DNA Genotype positivity and associated clinical features.

METHODOLOGY & MATERIALS

This descriptive observational quantitative study assessed the prevalence of HPV-DNA Genotype positivity and its association with various gynecological symptoms. The study population comprised married women aged 21 to 70 who presented to the outpatient chamber of Prof. Dr. Sabera Khatun, a renowned gynecological oncologist at Central Hospital, Dhaka, Bangladesh, between Jan 2017 and Jan 2021. A total of 244 samples were collected for HPV – genotyping from women who had never undergone cervical cancer screening, had irregular screening, or attended follow-up visits after getting for cervical intraepithelial neoplasia or other preinvasive cervical conditions. Relevant institutional authorities obtained ethical clearance for retrospective data collection, and patient anonymity was maintained throughout the research process. The study adhered to the principles of the Declaration of Helsinki. This study was part of an opportunistic cervical cancer screening program and did not involve randomization. Inclusion criteria included adult married women within the age range with available HPV test reports and clinical data. Patients with a prior history of cervical cancer, hysterectomy, or incomplete clinical documentation were excluded.

Data were collected from prescriptions, laboratory reports, and clinical documentation, including demographic details, clinical symptoms, menstrual history, reproductive history, and HPV testing results. Data was collected manually by trained medical staff and later verified by physicians and statisticians for consistency and completeness. Cervical specimens were collected using standard gynecological procedures using a specially designed cervical swab with a detachable head. Samples were analyzed at accredited molecular pathology laboratories using the Smart Cycler II Real-Time PCR System (Cepheid, USA). Real-time PCR was performed with TaqMan probes targeting the E1-E2 region of the HPV genome to detect the presence of high-risk HPV genotypes, including types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. The method ensured high specificity and sensitivity in HPV-DNA genotype detection.

Collected data were initially compiled using Microsoft Excel 2016 and subsequently imported into IBM SPSS Statistics version 26.0 for statistical analysis. Descriptive statistics (frequency, percentage, median) were used to summarize the data. Cross-tabulations explored associations between HPV-DNA positivity and variables such as age, parity, menstrual cycle characteristics, gynecological abnormalities, and HPV genotype distribution. Statistical significance was assessed using chi-square tests and p-values, where applicable.

RESULT

The study included a diverse age range of participants, with the highest representation in the 36–40 age group (21.07%), followed by 31–35 (20.25%) and 41–45 (19.01%). HPV-DNA positivity was more prevalent among individuals aged 31–40, peaking in the 36–40 group (n=9) (Table 1, figure 2). Analysis of parity revealed a trend where higher parity (>2) showed greater HPV positivity (30.44%), suggesting a possible association between increased childbirth and HPV infection (Table 2). Cervical and genital abnormalities were more common among HPV-positive individuals (55.56%), indicating a significant correlation between visible gynecological abnormalities and HPV infection (Table 3). Among those who tested positive, the majority complained of dysmenorrhea (73%), though no significant difference was found when compared with HPV-negative individuals (Figure 3). Menstrual flow characteristics did not significantly differ by HPV status, with average flow being the most common in both groups (Table 4, Figure 4). The difference is not statistically significant. Similarly, regular menstrual cycles were common among both HPV-positive and negative patients, showing no statistically significant association (p=0.944) (Table 5). A majority of those with discharge and dysmenorrhea were HPV-positive, though not significantly different from HPV-negative counterparts (Table 6, Figure 5). Median age at marriage and duration of marriage also showed no significant association with HPV positivity (p=0.67 and p=0.31, respectively) (Table 7 & 8). Genotyping revealed that HPV-16 was the most common genotype (7.44%), followed by HPV-52 (2.07%) and HPV-68 (1.24%) (Table 9). High-risk types HPV-16 and 18 together constituted over half (55.56%) of all positive cases (Table 10).

Table 1: Age Distribution of Study Participants

Age group	Frequency (n)	Percentage (%)
23-25	3	1.24
26-30	30	12.40
31-35	49	20.25
36-40	51	21.07
41-45	46	19.01
46-50	25	10.33
51-55	16	6.61
56-60	12	4.96
>60	10	4.13

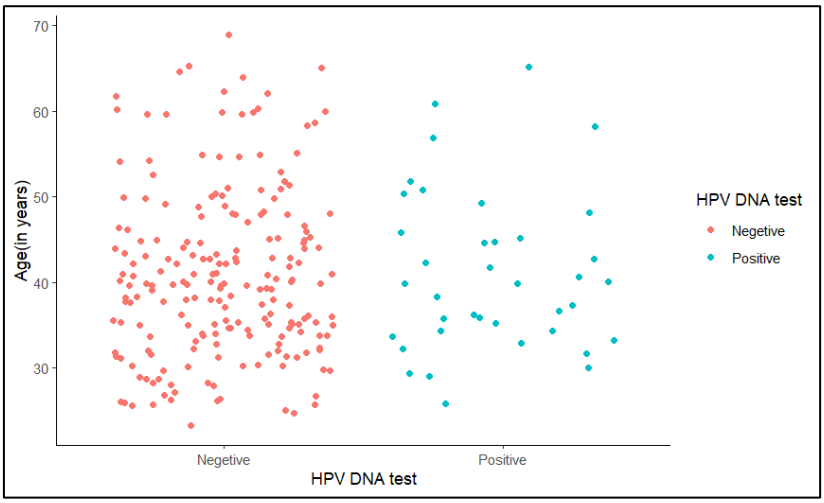

Figure 1: HPV-DNA positivity among study cases

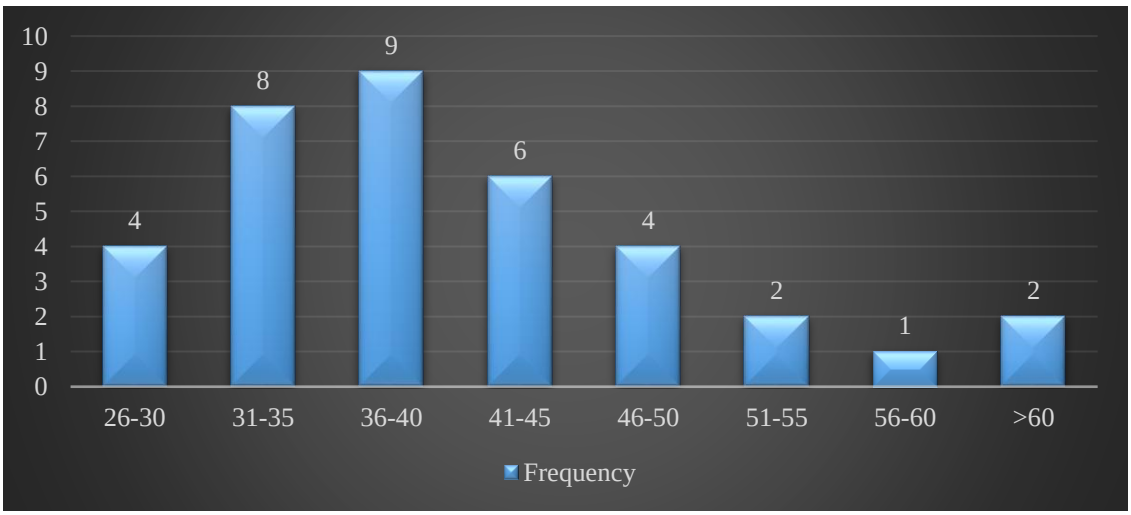

Figure 2: Frequency of HPV-DNA Positivity across Age Groups

Table 2: Association between Parity and HPV-DNA Test Results

Para	Positive		Negative	
	n	%	n	%
0	2	8.70	4	2.25
1	4	17.40	16	8.10
2	6	26.10	47	26.40
3	7	30.44	61	34.27
>3	4	17.40	50	28.09

Table 3: Cervical and External Genital Findings about HPV-DNA Test Results

External Genitalia and Cervix	Positive		Negative	
	n	%	n	%
Normal	12	44.44	74	38.74
Different abnormalities	15	55.65	117	16.25

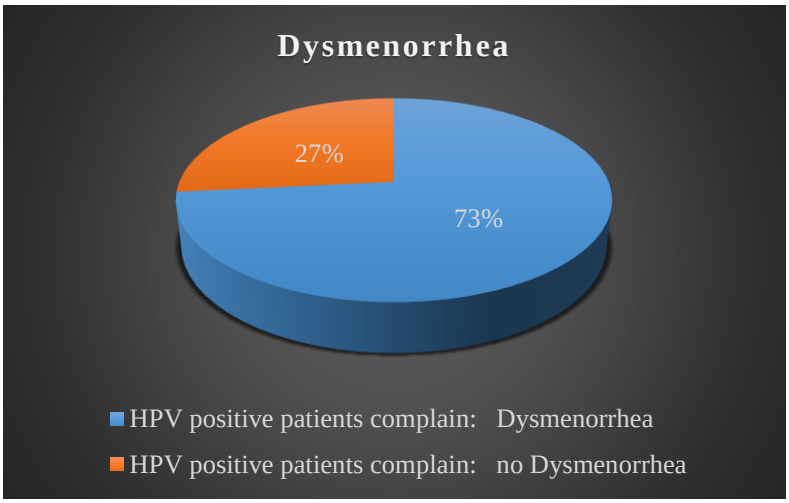

Figure 3: Dysmenorrhea Complaints among HPV-Positive Patients

Table 4: Association between Menstrual Flow and HPV-DNA Status

Menstrual Flow	Positive		Negative		P-value
	n	%	n	%	
Heavy	4	33.33	25	25.96	0.622
Average	7	58.33	57	54.81	
Scanty	1	8.33	20	19.23	

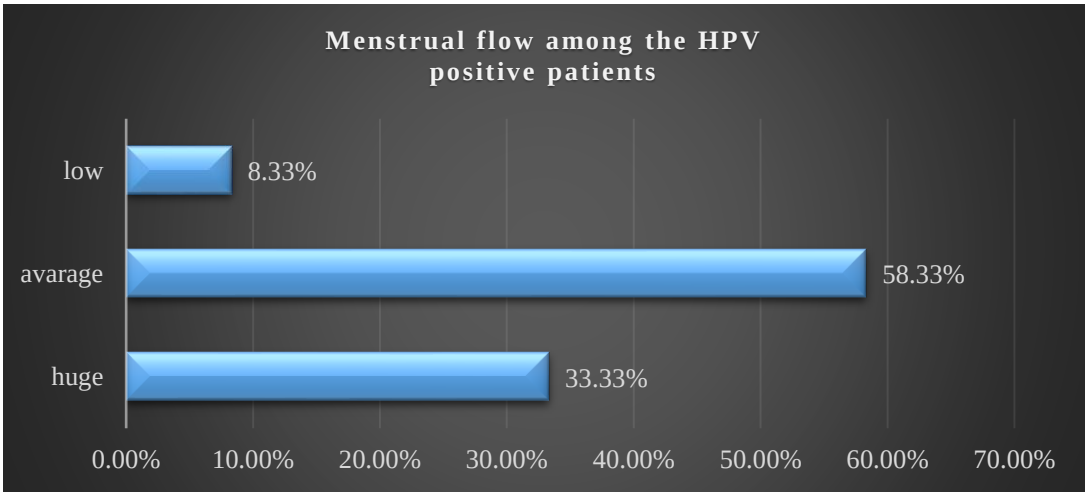

Figure 4: Distribution of Menstrual Flow Volume among HPV-Positive Patients

Table 5: Menstrual Cycle Regularity and HPV-DNA Test Results

Menstrual Cycle	Positive		Negative		P-value
	n	%	n	%	
Regular	11	57.89	88	54.32	0.944
Pause	3	15.79	30	18.52	
Irregular	5	26.32	44	27.16	

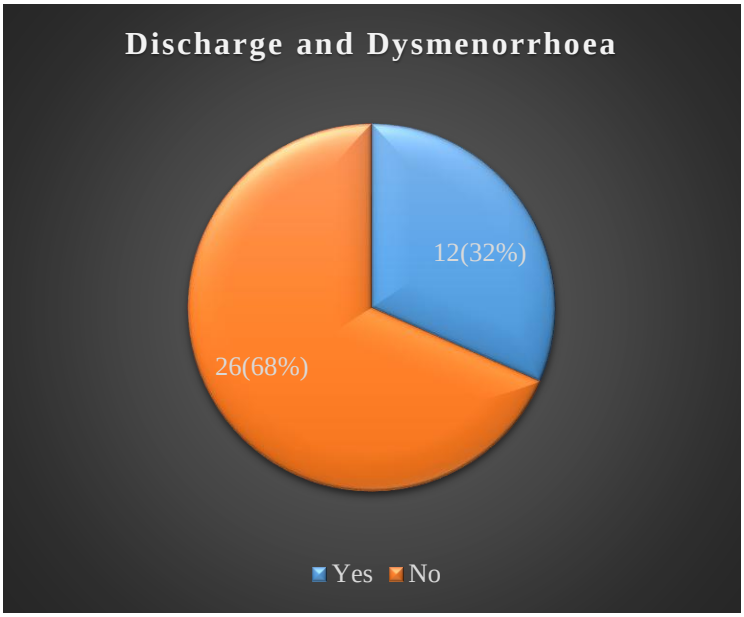

Figure 5: Association between Vaginal Discharge with Dysmenorrhea and HPV-DNA Positivity

Table 6: Relationship between Dysmenorrhea and HPV-DNA Status

Dysmenorrhea	Positive		Negative		P-value
	n	%	n	%	
Yes	8	72.73	77	74.04	1
No	3	27.27	27	25.96	

Table 7: Comparison of Age at Marriage between HPV-Positive and HPV-Negative Participants

Variable	HPV		P-Value
	Positive	Negative	
Median of the Age at which they got Marriage	19.5	18	0.67

Table 8: Comparison of Marriage Duration between HPV-Positive and HPV-Negative Participants

Variable	HPV		P-value
	Positive	Negative	
Married For (median in years)	17.5	20	0.31

Table 9: Distribution of HPV Genotypes among Participants

HPV	Frequency (n)	Percentage (%)
Negative	206	85.12
Genotype 16 positive	18	7.44
Genotype 52 positive	5	2.07
Genotype 68 positive	3	1.24
Genotype 51 positive	3	1.24
Genotype 56 positive	2	0.83
Genotype 18 positive	2	0.83
Genotype 39 positive	1	0.41
Genotype 45 positive	1	0.41
Genotype 66 positive	1	0.41

Table 10: Distribution of High-Risk HPV Genotypes (16 & 18) Versus Other Genotypes among HPV-Positive Cases

Genotype of HPV	Frequency (n)	Percentage (%)
16 & 18	20	55.56
Others	16	44.44

DISCUSSION

This study aimed to evaluate the prevalence of HPV-DNA positivity and its association with gynecological parameters and symptoms among women attending a tertiary care center in Bangladesh. The findings contribute essential insights into HPV epidemiology, symptomatology, and genotype distribution in the local context, where cervical cancer remains a significant public health concern. HPV-DNA positivity was most frequently observed in the 31–40 age group, particularly in the 36–40 range. This aligns with global trends indicating that HPV infection is most prevalent in sexually active women under the age of 45, especially those in their 30s and early 40s, who may have had prolonged exposure or persistent infections [9]. The higher infection rates in this age group underscore the importance of targeted screening and vaccination in reproductive-aged women. Parity appeared to be an influencing factor, with the highest HPV positivity (30.44%) observed among women with more than two childbirths. This supports existing literature suggesting that high parity may increase the risk of persistent HPV infection and cervical neoplasia due to hormonal and immunological changes, as well as cervical trauma during childbirth [10]. Moreover, HPV-positive women in this study were more likely to exhibit visible abnormalities in the external genitalia and cervix (55.56%), suggesting a clinically observable correlation between HPV infection and lower genital tract pathology. This finding is consistent with previous studies where HPV was significantly associated with cervical epithelial abnormalities detected via colposcopy or Pap smear [11]. Though a majority of HPV-positive women reported dysmenorrhea (73%) and discharge, these symptoms did not significantly differ from HPV-negative individuals. This reinforces the known characteristic of HPV infection, often being asymptomatic or presenting with non-specific symptoms, making routine screening imperative for early detection [12]. Menstrual patterns, including flow and regularity, showed no significant association with HPV status, indicating that such features may not be reliable clinical indicators of HPV infection. Marriage-related factors, such as median age at marriage and duration of marriage, also showed no significant correlation with HPV positivity. However, early age at marriage and prolonged sexual exposure are considered indirect risk factors for HPV acquisition in broader epidemiological studies [13]. This disparity may reflect cultural or demographic nuances in the Bangladeshi population, warranting further investigation. Genotype analysis revealed that HPV-16 was the most common variant (7.44%), followed by types 52 and 68. HPV types 16 and 18 covered by the currently administered bivalent vaccine (Cervarix®) accounted for over half (55.56%) of all infections. This suggests that the national vaccination program may significantly reduce the burden of HPV-related cervical disease. However, the presence of other high-risk genotypes (44.44%), such as types 52, 51, and 68, highlights the potential value of introducing broader coverage vaccines like the nonavalent vaccine (Gardasil 9®) in the future [14].

Limitations of the study:

The study was conducted in a single private outpatient setting, which may not represent Bangladesh's broader population. The sample size was small and limited to women seeking care, introducing potential selection bias. Data were collected retrospectively from prescriptions and lab reports, possibly leading to incomplete or inconsistent information. Additionally, the study lacked long-term follow-up data to assess the progression of HPV infection or response to treatment.

CONCLUSION AND RECOMMENDATIONS

Human Papillomavirus (HPV) infection, the primary cause of cervical cancer, is preventable through timely vaccination with an effective, genotype-specific vaccine. This study emphasizes the need for larger-scale research to identify the predominant HPV genotypes circulating in Bangladesh, which can guide the selection and implementation of the most appropriate vaccines. Regular cervical cancer screening is crucial for early detection of pre-invasive lesions, enabling prompt treatment and significantly reducing the risk of cancer progression. Strengthening awareness, vaccination programs, and screening initiatives will play a pivotal role in lowering the cervical cancer burden among Bangladeshi women.

Funding: *No funding sources*
Conflict of interest: *None declared*

REFERENCES

1. World Health Organization. WHO technical guidance and specifications of medical devices for screening and treatment of precancerous lesions in the prevention of cervical cancer. World Health Organization; 2020 May 11.
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2018 Nov;68(6):394-424.
3. de Sanjose S, Quint WG, Alemany L, Geraets DT, Klaustermeier JE, Lloveras B, Tous S, Felix A, Bravo LE, Shin HR, Vallejos CS. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. The lancet oncology. 2010 Nov 1;11(11):1048-56.
4. Hu B. Classification of papillomaviruses (PVs) based on 189 PV types and proposal of taxonomic amendments. Virology. 2010; 401:70-9.
5. 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. New England journal of medicine. 2003 Feb 6;348(6):518-27.
6. World Health Organization. Human papillomavirus vaccines: WHO; 2020 December.
7. World Health Organization. Global strategy to accelerate the elimination of cervical cancer as a public health problem. World Health Organization; 2020 Dec 31.
8. Khatun S. History of introduction of bivalent human papilloma virus 16/18 vaccine in Bangladesh. Bangladesh Journal of Obstetrics & Gynaecology. 2019 Sep 30;34(2):68-70.
9. Bruni L, Diaz M, Barrionuevo-Rosas L, Herrero R, Bray F, Bosch FX, de Sanjosé S, Castellsagué X. Global estimates of human papillomavirus vaccination coverage by region and income level: a pooled analysis. The Lancet global health. 2016 Jul 1;4(7):e453-63.
10. 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. New England journal of medicine. 2003 Feb 6;348(6):518-27.
11. Schiffman M, Doorbar J, Wentzensen N, De Sanjosé S, Fakhry C, Monk BJ, Stanley MA, Franceschi S. Carcinogenic human papillomavirus infection. Nature reviews Disease primers. 2016 Dec 1;2(1):1-20.
12. de Sanjose S, Brotons M, Pavon MA. The natural history of human papillomavirus infection. Best practice & research Clinical obstetrics &gynaecology. 2018 Feb 1;47:2-13.
13. Vaccarella S, Herrero R, Dai M, Snijders PJ, Meijer CJ, Thomas JO, Hoang Anh PT, Ferreccio C, Matos E, Posso H, De Sanjosé S. Reproductive factors, oral contraceptive use, and human papillomavirus infection: pooled analysis of the IARC HPV prevalence surveys. Cancer Epidemiology Biomarkers & Prevention. 2006 Nov 1;15(11):2148-53.
14. Moreira ED, Block SL, Ferris D, Giuliano AR, Iversen OE, Joura EA, Kosalaraksa P, Schilling A, Van Damme P, Bornstein J, Bosch FX. Safety profile of the 9-valent HPV vaccine: a combined analysis of 7 phase III clinical trials. Pediatrics. 2016 Aug 1;138(2).