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Characteristics and Related Factors of High-Risk Human Papillomavirus Infection in Pregnant Women

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Background: Cervical cancer is a risk for women worldwide. The aim of this study was to examine the occurrence of high-risk human papillomavirus (HR-HPV) infection and its related factors in pregnant women and provide a scientific basis for the targeted prevention and treatment of cervical cancer in pregnant women.





Material/Methods: A total of 1774 pregnant women were included, and 1774 non-pregnant women were selected as controls. Cervical exfoliated cells were collected from all women for HR-HPV (AptimaE6, E7mRNA) and ThinPrep cytologic testing, and the vaginal discharge of all pregnant women was tested for pH level and routine pathogenic microorganisms.

Results: The HPV-16-positive and HPV-16/18/45-positive rates in pregnant women were higher than those of non-pregnant women ($P < 0.05$). There was a statistically significant difference in HR-HPV-positive rate, HPV-16-positive rate, and non-HPV-16/18/45-positive rate among pregnant women of different ages ($P < 0.05$). There was a statistically significant difference in HR-HPV-positive rate and non-HPV-16/18/45-positive rate in the first, second, and third trimester ($P < 0.05$). The HR-HPV-positive rate, HPV-16-positive rate, HPV-18/45-positive rate, and non-HPV-16/18/45-positive rate of pregnant women with concurrent infection were higher than those in women without concurrent infection ($P < 0.05$). The HR-HPV-positive and HPV-16/18/45-positive rates in pregnant women were associated with cytologic examination results ($P < 0.05$).

Conclusions: The overall infection rates of HR-HPV-16 and HR-HPV-18/45 in pregnant women were higher than those in non-pregnant women. The gestation period was found to be a susceptible period for infection with HR-HPV, and we recommend the implementation of cervical cancer screening based on HR-HPV testing in pregnant women.

Keywords: **Human papillomavirus 16 • Human papillomavirus 18 • Pregnancy • Vaginal Discharge**

Full-text PDF: <https://www.medscimonit.com/abstract/index/idArt/929100>

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Background

Cervical cancer ranks fourth in cancers of women for both incidence and mortality across the world [1]. According to World Health Organization statistical data, about 75 000 new cases of cervical cancer occur in China every year [2]. Studies have confirmed that human papillomavirus (HPV) plays a key role in the development of cervical cancer. It is the most common sexually transmitted virus in the world, with more than 150 subtypes [3]. HPV genital tract infection is subclassified into low-risk subtypes (6, 11, 42, and 43) and high-risk subtypes (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59), according to their potential risk of causing malignant diseases. High-risk HPV (HR-HPV) subtypes such as HPV subtype 16 (HPV-16) and HPV-18 are considered the main viruses associated with malignant diseases such as cervical cancer, vaginal cancer, vulvar cancer, anal cancer, and head and neck cancer [4], and HPV-16 is the most common subtype in women who have HPV, followed by HPV-18 [5]. The HPV-16 and HPV-18/45 subtype test (Aptima HPV-GT) is a qualitative E6/E7 oncogene messenger RNA test that can detect HPV-16, HPV-18, and HPV-45.

Young women (<30 years of age) are at the greatest risk of HPV infection, although most of them have no clinical symptoms and can clear the virus through their strong immune systems. However, in developing countries, the majority of pregnancies occur in women under the age of 30 years; therefore, these women are suitable for cervical cancer screening. There are few cervical cancer screenings performed for pregnant women in China at present for reasons including China's national conditions, patients' insufficient knowledge of cervical cancer and precancer, and pregnant women's fear of miscarriage and refusal to have vaginal examination. In addition, there are few targeted studies on the occurrence and influencing factors of HPV infection in this population of women. The purpose of this study was to target pregnant women who receive antenatal care in the hospital, analyze the occurrence and related factors of HR-HPV infection in pregnant women, and provide a scientific basis for an appropriate prevention strategy of cervical cancer in these women.

Material and Methods

Study Population

Pregnant women who received antenatal care at the Huzhou Maternal & Child Health Care Hospital in Zhejiang Province from January 2018 to January 2020 and met the following conditions were enrolled into the study: no history of cervical cancer or precancer or history of other malignant tumors; no history of cervical surgical treatment; not in the active period of autoimmune diseases or taking long-term oral immunosuppressor

medication; aged between 20 and 44 years; no liquid-based thin-layer cytology (TCT) or HPV test within the past year; no pathological gestation such as placenta previa or vasa previa; and agreed to participate in this study voluntarily and signed informed consent. During this period, a total of 22 133 pregnant women received antenatal care in our hospital, of which 1774 met the above conditions and were included in the study.

Non-pregnant women who received health examinations in our hospital during the same period were selected as controls when they met the following criteria: no history of cervical cancer or precancer or history of other malignant tumors; no history of cervical surgical treatment; not in the active period of autoimmune diseases or taking long-term oral immunosuppressor medication; not pregnant; and agreed to participate in this study voluntarily. At a 1: 1 ratio, 1774 age-matched non-pregnant women were selected randomly as controls, according to a random numbers table of the clinic visiting order. **Figure 1** shows the flow chart of the test.

Experimental Ethics

The study was approved by the Ethics Committee of Huzhou Maternal & Child Health Care Hospital (Ethics Committee No. 2019-018; Chairperson, Pingya He), and written informed consent was provided by all patients before enrollment in the study.

Test Reagent and Method

For the detection of HR-HPV, cervical exfoliated cells were collected, and Aptima HPV and Aptima HPV-GT test kits (Hologic Corporation, USA) were used to test for the 14 high-risk HPV subtypes specified by the International Agency for Research on Cancer, according to the manufacturer's instructions. The following were detected: HPV subtypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. For specimens that tested positive by the Aptima HPV test, the Aptima HPV-GT test kit was used to further detect HPV subtyping (16,18/45). For specimens that tested negative by the Aptima HPV test, the Aptima HPV-GT test was also regarded as negative.

For the cytological examination, cervical exfoliated cells were collected, and 1 mL of cervical exfoliated cell preservation solution was used for the Aptima HPV test. The fully automatic ThinPrep 2000 liquid-based cytology processor (Hologic Corporation, USA) was used to make liquid-based thin-layer cell sheets out of the remaining preserved solution and to conduct the cytologic examinations, according to the instruction manual. The cytological diagnoses were made according to the Bethesda system [6], proposed in 2014.

Next, vaginal discharge pH levels and common pathogenic microorganisms were detected. The physiological saline containing

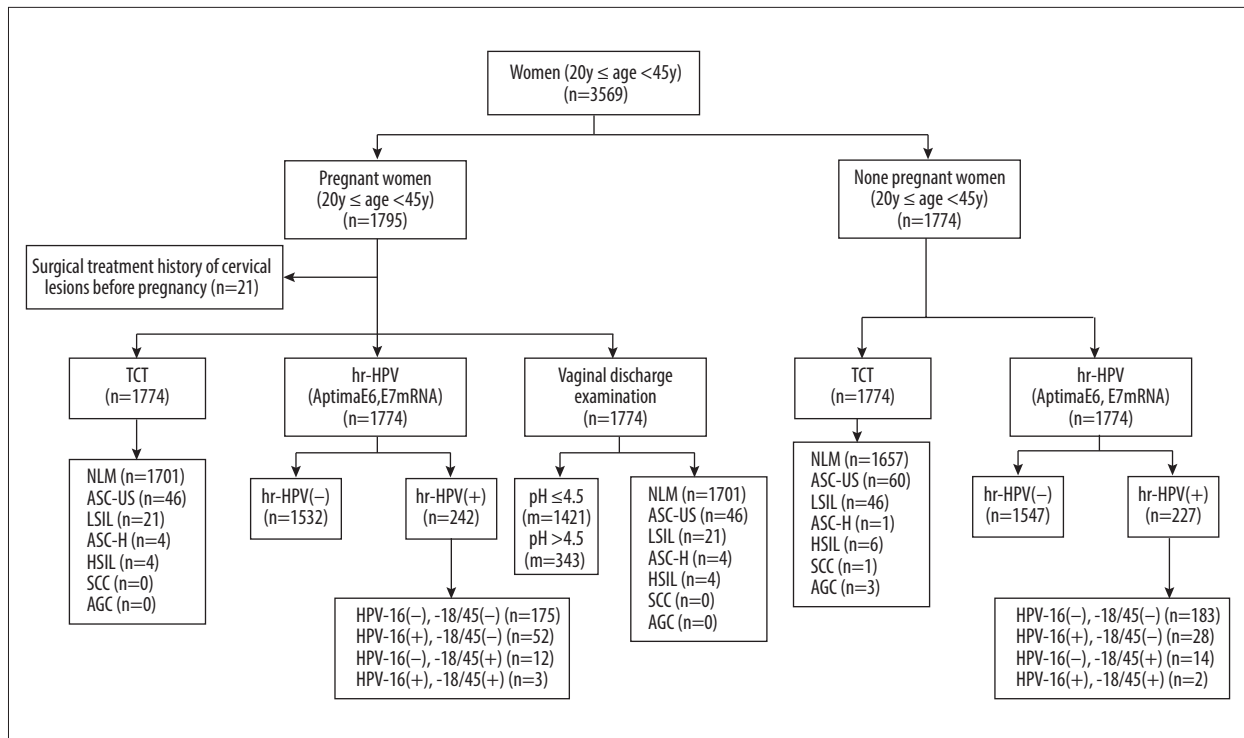


Figure 1. Flow chart of the test. NILM – no intraepithelial lesion or malignancy; ASCUS – abnormal squamous cells of uncertain significance; LSIL – low-grade squamous intraepithelial lesion; ASC-H – atypical squamous cells, cannot exclude HSIL; HSIL – high-grade squamous intraepithelial lesion; SCC – squamous cell carcinoma; AGC – atypical glandular cells; VVC – vulvovaginal candidiasis; BV – bacterial vaginosis; TV – trichomonas vaginalis.

vaginal discharge was evenly spread on a sterile glass slide. A Nissan Olympus optical microscope was used to confirm the view field under 10× magnification and to observe 10 to 15 fields. Using the microscope under 40× magnification, the hyphae, spores of *Candida albicans*, trichomoniasis, and clue cells were found and observed. Precision pH test strips were used to determine the pH value of vaginal discharge. The diagnostic criteria strictly followed the third edition of the *National Guide to Clinical Laboratory Procedures* [7].

Statistical Method

SPSS version 22.0 was used for statistical analysis. The independent *t* test was used for measurement data, and the Pearson χ^2 test was used for count data, where $P < 0.05$ was considered to represent a statistically significant difference. If $P < 0.05/n$ when comparing multiple sets of data in pairs, the difference was considered statistically significant (*n* is the number of groups compared in pairs).

Results

The Rate of HR-HPV Infection in Pregnant Women and Non-Pregnant Women

The average age of the 1774 women in the pregnant group was 27.9 ± 5.3 years, and the average age of the 1774 women in the non-pregnant group was 28.3 ± 5.3 years. There was no significant difference in age between the 2 groups. **Figure 2** shows the positive rates of HR-HPV and HPV-16/18/45 in the 2 groups, while **Figure 3** illustrates the statistics for each age group comparison between pregnant women and non-pregnant women.

There were statistically significant differences in HR-HPV-positive rate, HPV-16-positive rate, and non-HPV-16/18/45 positive rate among pregnant women in all age groups ($P < 0.05$). **Figure 4** shows the comparison of each age group. There was no significant difference in the HPV-18/45-positive rate among pregnant women of all ages.

TCT Results of Pregnant Women and Non-Pregnant Women of Different Ages

Table 1 shows the rates and the statistically significant differences in abnormal cytologic examination results in pregnant

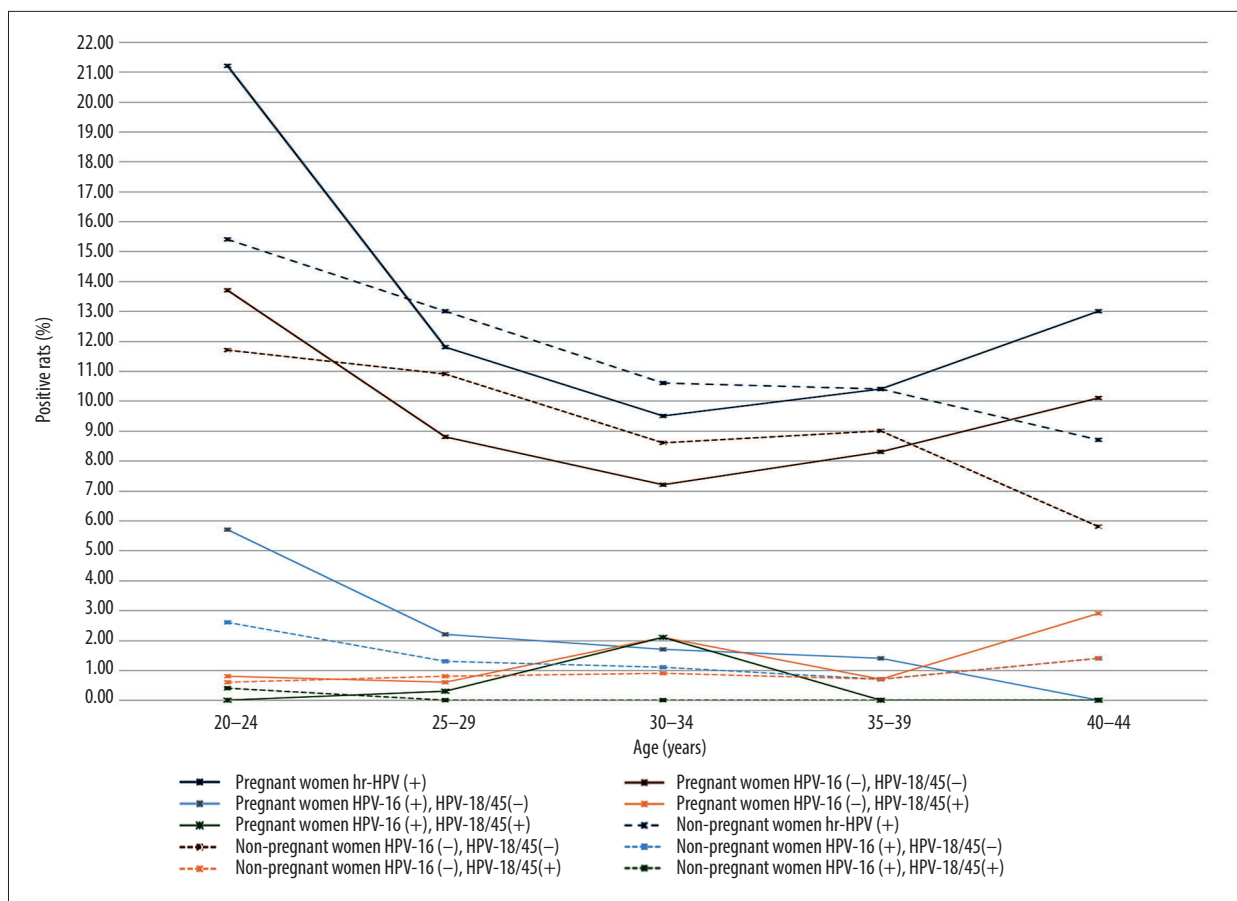


Figure 2. The positive rates of high-risk human papillomavirus (HR-HPV) and HPV subtype 16/18/45 in pregnant and non-pregnant women.

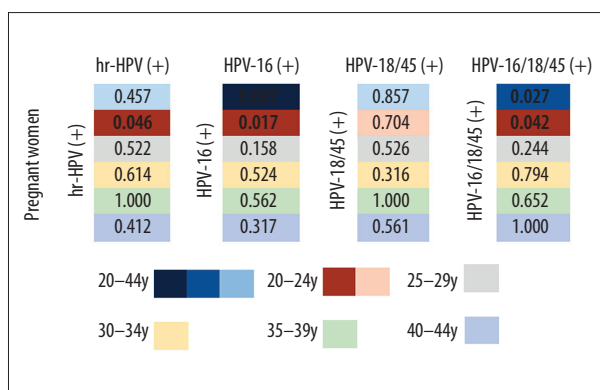


Figure 3. The differences in the positive rates of high-risk human papillomavirus (HR-HPV) and HPV subtype 16/18/45 between pregnant and non-pregnant women in each age group.

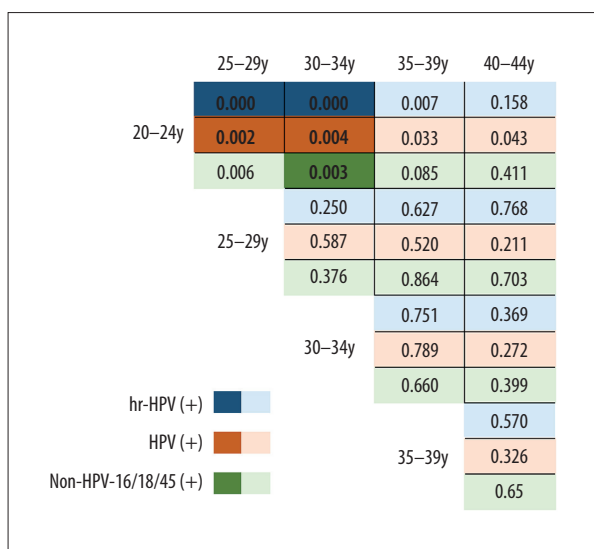


Figure 4. The difference in the positive rate of high-risk human papillomavirus (HR-HPV), HPV subtype 16 (HPV-16) and non-HPV-16/18/45 in pregnant women by age group.

Table 1. Cervical cytology examination results of pregnant women and non-pregnant women by different age groups.

Age (y)	Pregnant women							Non-pregnant women							χ^2	P		
	Total	NILM	ASCUS	LSIL	ASC-H	HSIL	\geq ASCUS rate	Total	NILM	ASCUS	LSIL	ASC-H	HSIL	SCC			AGC	\geq ASCUS rate
20-24	495	464	20	11	0	0	6.3%	495	461	14	20	0	0	0	0	6.9%	0.148	0.700
25-29	718	696	16	5	1	0	3.1%	718	667	27	18	1	4	0	1	7.1%	12.138	0.000
30-34	348	333	8	4	1	2	4.3%	348	330	12	5	0	1	0	0	5.2%	0.286	0.593
35-39	144	140	1	1	2	0	2.8%	144	138	3	1	0	0	1	1	4.2%	0.413	0.520
40-44	69	68	1	0	0	0	1.4%	69	61	4	2	0	1	0	1	11.6%	5.782	0.016
Total	1774	1701	46	21	4	2	4.1%	1774	1657	60	46	1	6	1	3	6.6%	10.766	0.001

Table 2. Results of high-risk human papillomavirus testing in pregnant women in different gestational weeks.

Gestational week (weeks)	Total cases	hr-HPV (-)	hr-HPV(+)				hr-HPV positive rate	Non-HPV16 or 18/45 positive rate
			HPV16, 18/45(-)	HPV16(+), HPV18/45(-)	HPV16(-), HPV18/45(+)	HPV16(+), HPV18/45(+)		
First trimester (<14)	594	515	62	12	4	1	13.3%	10.4%
Second trimester (14-27+6)	980	830	104	37	7	2	15.3%	10.6%
Third trimester (\geq 28)	200	187	9	3	1	0	6.5%	4.5%
Total	1774	1532	175	52	12	3	13.6%	9.9%
χ^2							11.023	7.309
P							0.004	0.026

women and non-pregnant women. Pairwise comparison by age revealed that the abnormal rates of cytologic examination in non-pregnant women aged 25 to 29 years and 40 to 44 years were significantly higher than those of pregnant women in the same age groups ($P<0.05$), and there was no statistically significant difference in other age groups. There was no statistically significant difference in the abnormal rate of cytologic examination between pregnant women of all ages.

The Results of HR-HPV and Cytology Examination of Pregnant Women at Different Gestational Weeks

Among the 1774 pregnant women, 594 (33.5%) were in the first trimester (<14 weeks gestation), 980 (55.2%) were in the second trimester (14-27 weeks+6 days gestation), and 200 (11.3%) were in the third trimester (\geq 28 weeks gestation). **Table 2** shows the differences in the positive rates of HR-HPV and the differences in non-HPV-16/18/45 among the 3 trimesters. Pairwise comparison showed that the positive rates

of HR-HPV in women in the first and second trimesters were higher than those in the third trimester ($P<0.017$). Also, pairwise comparison showed that the positive rates of non-HPV-16 and non-HPV-18/45 in women in the first and second trimester were higher than those in the third trimester ($P<0.017$).

Table 3 shows the results of the cervical cytology examination of pregnant women and the difference among the 3 trimesters. There was an overall significant difference among the 3 trimesters ($P<0.05$) and also between the first and the third trimesters ($P=0.017$), but there was no statistically significant difference between the first and the second trimesters or the second and the third trimesters.

Correlation Between the Vaginal Discharge Examination and HR-HPV Infection in Pregnant Women

Tables 4 and 5 show the results of the vaginal discharge examination. The positive rate of HR-HPV in pregnant women

Table 3. Results of cervical cytology examination of pregnant women at different gestational weeks.

Gestational week (weeks)	Total	NILM	ASCUS	LSIL	ASC-H	HSIL	≥ASCUS rate
First trimester(<14)	594	566	18	5	3	2	4.7%
Second trimester(14-27 ⁺⁶)	980	937	27	15	1	0	4.4%
Third trimester (≥28)	200	198	1	1	0	0	1.0%
Total	1774	1701	46	21	4	2	4.1%
χ^2							6.598
<i>P</i>							0.036

Table 4. The effect of pH value of vaginal secretion on high-risk human papillomavirus infection in pregnant women.

Vaginal discharge examination	Total	hr-HPV (-)	hr-HPV(+)				hr-HPV positive rate	Non-HPV16 or 18/45 positive rate
			HPV16, 18/45(-)	HPV16(+), HPV18/45(-)	HPV16(-), HPV18/45(+)	HPV16(+), HPV18/45(+)		
pH ≤4.5	1431	1292	97	33	7	2	9.7%	6.8%
pH >4.5	343	240	78	19	5	1	30.0%	22.7%
Total	1774	1532	175	52	12	3	13.6%	9.9%
χ^2							96.934	79.283
<i>P</i>							0.000	0.000

Table 5. The influence of vaginal secretion infection on high-risk human papillomavirus infection in pregnant women.

Vaginal discharge examination	Total	hr-HPV (-)	hr-HPV(+)				hr-HPV positive rate	Non-HPV16 or 18/45 positive rate
			HPV16, 18/45(-)	HPV16(+), HPV18/45(-)	HPV16(-), HPV18/45(+)	HPV16(+), HPV18/45(+)		
No co-infection	1677	1469	154	43	9	2	12.4%	9.2%
VVC	51	37	9	3	2	0		
BV	35	21	8	4	1	1		
TV	7	4	1	2	0	0		
VVC+BV	1	0	1	0	0	0		
BV+TV	3	1	2	0	0	0		
Total co-infected persons	97	63	21	9	3	1	35.1%	21.6%
χ^2							39.926	16.027
<i>P</i>							0.000	0.000

with a vaginal discharge pH level >4.5 was higher than those with pH ≤4.5 (*P*<0.05). The positive rate of HPV-16 in pregnant women with pH >4.5 was significantly higher than that of the pregnant women with pH ≤4.5 (*P*<0.05). There was no significant difference between the HPV-18/45-positive rates in the 2 groups. The HPV-16/18/45-positive rate in pregnant

women with a pH level >4.5 was higher than that of the pregnant women with a pH ≤4.5 (*P*<0.05). The non-HPV-16-positive or non-HPV-18/4-positive rates in pregnant women with a pH >4.5 were significantly higher than in the pregnant women with a pH ≤4.5 (*P*<0.05). The positive rate of HR-HPV in pregnant women with concurrent vaginal infection was significantly

Table 6. High-risk human papillomavirus test results of women with different cervical cytological diagnoses.

Cervical cytological diagnosis	Total	hr-HPV (-)	hr-HPV(+)				hr-HPV positive rate	Non-HPV16 or 18/45 positive rate
			HPV16, 18/45(-)	HPV16(+) HPV18/45(-)	HPV16(-) HPV18/45(+)	HPV16(+) HPV18/45(+)		
NILM	1701	1510	139	40	10	2	11.2%	3.1%
ASCUS	46	21	20	4	0	1	54.3%	10.9%
LSIL	21	1	14	5	1	0	95.2%	28.6%
ASC-H	4	0	2	2	0	0	100%	50.0%
HSIL	2	0	0	1	1	0	100%	100%
Total	1774	1532	175	52	12	3	13.6%	3.8%
χ^2							218.82	118.790
<i>P</i>							0.000	0.000

higher than that in pregnant women without concurrent infection ($P < 0.05$). The HPV-16-positive rate, HPV-18/45-positive rate, and non-HPV-16/18/45-positive rate of pregnant women with concurrent vaginal infection were higher than those of pregnant women without concurrent infection ($P < 0.05$).

Correlation Between the Result of Cervical Cytological Examination and HR-HPV Infection in Pregnant Women

Table 6 shows the HR-HPV test results of women with different cervical cytological diagnoses. Among the 1774 pregnant women, the cytological examination results of 1701 (95.9%) patients were negative for intraepithelial lesion or malignancy (NILM), 46 (2.6%) patients had atypical squamous cells of undetermined significance (ASCUS), 21 (1.2%) patients had low-grade squamous intraepithelial lesions (LSIL), 4 (0.2%) patients had atypical squamous cells, which cannot exclude high-grade squamous intraepithelial lesions (HSIL) (ASC-H), and 2 (0.1%) patients had HSIL. The positive rate of HR-HPV and the total positive rate of HPV-16 and HPV-18/45 increased significantly with cervical cytological diagnosis ($P < 0.05$).

Among the 1774 pregnant women, 390 (22.0%) had vaginal bleeding from the cervix when cervical exfoliation cytology samples were taken. The blood volume was about 3 mL to 7 mL, and bleeding stopped within 5 min after pressure was applied with a cotton swab. There were no cases of miscarriage or infection. A total of 262 of the pregnant women were HR-HPV-positive and/or had an abnormal cytological examination, among which 6 had LSIL and were HR-HPV-16/18/45-positive, and another 6 had ASC-H or worse. All 12 of these patients refused colposcopy examination during pregnancy for fear of miscarriage. Seventy-one women had not delivered at the time of this report, and 58 pregnant women were lost to follow-up for reasons including phone number changes and

delivering at local hospitals. Seventy-nine patients were reviewed for HPV and/or cytological examination on the 42nd postpartum day, and the results of those who previously had cytological examination results of ASCUS had all changed to NILM. Sixty-five patients changed to HR-HPV-negative, 10 patients were still non-HPV-16/18/45-positive, 1 patient who had been HPV-16-positive changed to non-HPV-16/18/45-positive, and 3 patients who were non-HPV-16/18/45-positive became HPV-16-positive. Fifty-four patients underwent colposcopy examination at 1 to 3 months postpartum, and a cervical biopsy was performed when necessary. Among them, 38 patients' colposcopy examinations indicated cervicitis, 9 indicated LSIL, and 8 indicated HSIL. These patients underwent further cervical conization, and the postoperative specimens were consistent with the colposcopy-directed biopsy.

Discussion

The positive rate of HPV varies greatly in many studies due to differences in the included population, detection method, and experimental design. Research shows that the HPV-positive rate in the general population in some areas of China ranges from 13.3% to 18.4% [8], while the reported HPV-positive rate in the reproductive tract in pregnant women is between 5.4% and 37.2% [9]. To date, many observational studies reported HPV infection during pregnancy, but the results are inconsistent. Some studies reported that the infection rate of HPV in pregnant women is higher than that in non-pregnant women [10] because of the mild immunosuppressive state during pregnancy. However, other reports showed no difference in the HPV-positive rate between pregnant and non-pregnant women [11]. The positive rate of HR-HPV in pregnant women in the present study was 13.6%, which is similar to the 12.5% of 1183 pregnant women reported by Takakuwa et al [12], who

also showed no significant difference in the HR-HPV-positive rate of 12.8% in non-pregnant women. In the present study, the positive rate of HR-HPV in pregnant women in the age group of 20 to 24 years was higher than that of non-pregnant women in the same age group. The rate of single HPV-16-positive and overall HPV-16/18/45-positive rates in pregnant women were higher than that in non-pregnant women. Schulze et al [13] reported that the positive rate of HR-HPV during pregnancy, especially of HPV-16, was significantly higher than that of non-pregnant women. This is consistent with the results of our study. The frequency of sexual activity during pregnancy is not high, so the reason for the increase of the positive rate of HPV-16 and other HR-HPVs may be the increase in pregnancy-related hormones and the selective activation of these viruses by immune factors, or the changes in the hormone environment and immune response may be beneficial to HPV infection and its persistent existence [14].

Our study showed that there were statistically significant differences in the HR-HPV-positive rate, HPV-16-positive rate, HPV-16/18/45-positive rate, and non-HPV-16/18/45-positive rate among pregnant women in all age groups. Both the HR-HPV-positive rate and HPV-16-single-positive rate were highest in the age group of 20 to 24 years. Some studies found that HPV infection was negatively correlated with age. The highest positivity rate is observed in 20- to 24-year-old women, and the rates decrease with age [9,15]. Takakuwa et al [12] also confirmed that the HPV infection rate of pregnant women <25 years is significantly higher than that of the women aged >25 years, the same phenomenon seen in non-pregnant women, which may be due to more frequent sexual activity or more sexual partners in this age group than in older women. Some studies [5] found that there was a double-peak of HPV infection. The first peak appears in women < 25 years old, and the second peak appears in women ≥ 44 years old. One reason for the second peak in non-pregnant women may be changes in hormone levels during the perimenopausal period. Another reason may be changes in sexual behaviors of women of this age group and their partners. A woman's pregnancy occurs during a specific age span. Few women give birth over the age of 45, and not many women given birth over the age of 40. In this study, there were 69 patients in the age group of 40 to 44 years, with a positive rate of HR-HPV of 13%.

Some studies have reported that the positive rates of HPV in the first and second trimesters are not higher than those in the third trimester [11]. Banura et al [16] reported that the positive rates of HPV in the first and second trimester were comparable to those in the third trimester, while Liu et al [9] reported that the infection rates of HPV in the 3 trimesters showed a "V" trend. However, in the present study, the positive rates of HR-HPV were significantly higher in the first and second trimesters than they were in the third trimester, and were the

highest in the second trimester. This may be correlated to the decrease of the immune response to HPV infection in the first and second trimesters and the rebound of the immune response to HPV infection and the increased clearance ability in the third trimester. However, the HPV infection rate in each trimester is still controversial, and more studies are needed.

Vaginal microbiota play an important role in protecting women's health. A healthy vaginal microbiome is mainly composed of *Lactobacillus*, which usually exists on the vaginal epithelial cells, can decompose the glycogen of the vaginal mucosal epithelial cells, produce a certain amount of lactic acid, and maintain the normal acidic environment of the vagina with a pH level between 3.8 and 4.5. *Lactobacillus* is reduced when there is vaginal dysbiosis and the pH level is >4.5 ; as a consequence, bacterial vaginosis, vulvovaginal candidiasis, and other infections occur and can lead to an increase in HPV infection [17]. Bacterial vaginosis and persistent HPV infections are significantly correlated [18]. Gillet et al [19] found that bacterial vaginosis and HPV infection are positively correlated. Chen et al [20] reported that bacterial vaginosis and trichomonas vaginalis increase the risk of HPV infection. Several studies reported that vaginal inflammation changed the normal intra-vaginal environment, which increases women's risk of sexually transmitted infections [21]. Clarke et al [22] found that women with higher a vaginal pH level have a higher HPV-positive rate, but few reports focused on pregnant women. In the present study, the infection rate of HR-HPV in pregnant women with a pH level >4.5 was significantly higher than those with a pH level ≤ 4.5 , and the rate of HR-HPV infection among pregnant women with mixed vaginal infections was significantly higher than those without vaginal infections, results that are consistent with the research in non-pregnant women. However, some researchers think that due to the increase of estrogen and menolipsis during pregnancy, the *Lactobacillus* in the vagina will become more abundant [23]. The infection of HR-HPV reduces the abundance of *Lactobacillus* in the vagina, leading to dysbiosis and various vaginal infections [24]. It cannot be determined from published research reports whether other vaginal infections cause an increase in HPV infection or whether HPV infection causes an increase in other infections; nevertheless, it is certain that there is a correlation between them.

In this study, the rate of cervical cytologic examination abnormality in pregnant women was 4.1%, which is consistent with the 2% to 7% abnormal rate reported by Hunter et al [25]. Cytology abnormality in our study was 4.7% in the first trimester and 4.4% in the second trimester, which are comparable to most studies; however, the 1.0% we found in the third trimester was significantly lower than that found in most studies. There were fewer women in the third trimester included in the present study for various reasons; therefore, this group may not be representative, owing to possible selection

bias. Non-pregnant women in our study had a rate of cytology abnormalities of 6.6%, higher than that of women during pregnancy. These results are consistent with the research by Wu et al [26]. The positive rate of HR-HPV and the total positive rate of HPV-16/18/45 in the present study were significantly increased with the upgrading of cytological diagnosis. This result is consistent with the results of most studies in non-pregnant women [27]. However, there are few large-scale studies on combined cytologic examination and HPV screening in pregnant women. Although the increased estrogen level during pregnancy moves the cervical columnar epithelium out to the portio vaginalis of the cervix, the basal cells in the cervical transformation zone can have nuclear enlargement and deep dyeing, and the transformation zone is more likely to change under the stimulation by physical damage, infection, and changes in vaginal pH level. This change is easily confused with cervical glandular epithelial cell atypia and increases the diagnosis rate of cervical intraepithelial neoplasia; however, the cytological examination during pregnancy is equivalent to that in the non-pregnancy period [28]. Brun-Micaleff et al [29] also reported that cervical cytological examination during pregnancy was effective and worth recommending.

Conclusions

Implementing population-based screening programs can significantly reduce cancer mortality and morbidity, especially for breast cancer, cervical cancer, and colorectal cancer [30]. In recent years, the age of occurrence of cervical cancer has become lower. For women who do not participate in a cervical cancer screening program, pregnancy is an opportunity for screening, with the prenatal examination clinics being ideal screening places. Pregnancy is a special physiological state, which is more likely to be affected by HR-HPV; therefore, it is most important to receive a cervical cancer screening consisting of combined cytologic examination and HR-HPV testing during pregnancy. However, this study was a cross-sectional study, and the persistence, clearance rate, and consequences of HPV infection are not fully elucidated. For patients with positive HR-HPV and/or an abnormal TCT, we need to perform further follow-up to guide the treatment of abnormal cervical cancer screening results during and after pregnancy.

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Conflicts of Interest

None.

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