Article

Discovery Medicine 2024; 36(184): 981–991
https://doi.org/10.24976/Discov.Med.202436184.91

Genotype Distribution and Prevalence of High-Risk Human Papillomavirus among Pregnant Women and Maternal-Fetal Pregnancy Outcomes in a Tertiary Hospital in Beijing, China

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Published: 20 May 2024

Background: High-risk human papillomavirus (HR-HPV) infection is the primary reason for cervical cancer and precancerous lesions in females. Specific immune alterations in pregnancy led to greater HR-HPV replication and reduced clearance of HR-HPV infection. This study retrospectively obtained and analyzed data from a tertiary hospital in Beijing, China. We aimed to ascertain both the genotype distribution and prevalence of HR-HPV in pregnant females. Moreover, we sought to analyze the association of HR-HPV with maternal-fetal pregnancy outcomes.

Methods: The retrospective observational cohort study was divided into two parts. Part I evaluated the genotype distribution and prevalence of HR-HPV. It encompassed 6285 pregnant women who underwent a routine pregnancy check-up, Thin Prep cytology test (TCT), and HR-HPV diagnosis during weeks 12–14 of gestation between January 1, 2013, and December 31, 2021. Part II analyzed the association between HR-HPV infection and maternal-fetal pregnancy outcome. Through a nearest-neighbor 1:1 propensity score matching (PSM), we matched HR-HPV-positive and HR-HPV-negative pregnant women using caliper width equal to 0.02. After PSM, 171 HR-HPV-positive and 171 HR-HPV-negative pregnant women were included to analyze the association between HR-HPV infection and maternal-fetal pregnancy outcome.

Results: In total 737 (11.73%) pregnant women were HR-HPV positive. The five most common genotypes of HR-HPV were HPV-52 (2.90%), HPV-58 (2%), HPV-16 (1.94%), HPV-51 (1.38%), and HPV-39 (1.29%). As for age-specific HPV prevalence, a "U-shaped" pattern was observed. The first and second peaks were detected in pregnant females aged $<$25 years and those aged $\geq$35 years, respectively. Our study found no significant difference between the HR-HPV-positive and the HR-HPV-negative pregnant females in the following maternal-fetal pregnancy outcomes: spontaneous abortion (1.2% for HR-HPV positive, 0% for HR-HPV negative, $p = 0.478$), preterm delivery (4.7% for HR-HPV positive, 5.3% for HR-HPV negative, $p = 0.804$), premature rupture of membrane (28.8% for HR-HPV positive, 22.8% for HR-HPV negative, $p = 0.216$), preeclampsia (7.6% for HR-HPV positive, 7.6% for HR-HPV negative, $p = 1$), oligohydramnios (8.2% for HR-HPV positive, 7% for HR-HPV negative, $p = 0.683$), fetal growth restriction (1.8% for HR-HPV positive, 0.6% for HPV negative, $p = 0.615$), placenta previa (1.2% for HR-HPV positive, 0.6% for HR-HPV negative, $p = 1$), postpartum hemorrhage (8.9% for HR-HPV positive, 11.2% for HR-HPV negative, $p = 0.47$). There was also no significant difference in delivery mode or birth weight between the two groups.

Conclusions: HPV-16, 52, and 58 were the most prevalent infection genotypes in pregnant females. The study showed no significant differences between HR-HPV-positive and HR-HPV-negative groups in the maternal-fetal pregnancy outcomes.

Keywords: high-risk human papillomavirus; genotype distribution; maternal-fetal pregnancy outcome

Introduction

Cervical cancer (CC), a potentially lethal type of genital tumor, is the fourth most frequently diagnosed type of cancer. It is also the fourth leading contributor to cancer-related mortality in females globally [1]. Around 604,127 new cases of CC and 341,831 deaths were observed globally in 2020 [2]. As per the data obtained from the World Health Organization (WHO), CC holds the second position in terms of both incidence and death rate among females in China, following breast cancer [1,3]. It is already established that persistent human papillomavirus (HPV) infection is strongly linked to the risk of developing CC. As per their oncogenic potential for CC, HPV types leading to genital tract infections (GTIs) are classified into the low-risk HPV (LR-HPV) subtypes (HPV-6, 11, 42, and 43) versus high-risk HPV (HR-HPV) subtypes (HPV-16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59) [4].

An increasing incidence and death trend of CC has been reported, specifically in younger females and pregnant women [5]. This could be caused by the fact that pregnant females are more vulnerable to HPV infection owing to the

immunosuppressive role of their hormones [6,7]. There are few targeted studies relevant to the occurrence and associated risk factors for HPV in pregnant women. The impact of HPV infection on pregnancy outcomes is yet to be elucidated.

Furthermore, various studies have produced contradictory results. Some authors found no correlation between HPV and adverse pregnancy outcomes [8,9]. On the other hand, some established a link to several adverse pregnancy outcomes like preterm birth [10], spontaneous abortion [9,11], premature rupture of membranes (PROM) [12], pregnancy-induced hypertensive disorders, intrauterine growth restriction [13], low birth weight, and even death of the fetus [14,15]. These contrasting results could potentially be attributed to varying inclusion criteria as well as research techniques employed in these studies.

This study sought to fill these gaps by investigating the prevalence and other relevant aspects of HPV in pregnant females. It also attempted to examine the association of HR-HPV with maternal-fetal pregnancy outcomes.

Experimental Methods and Design

Study Design

Part I

We retrospectively examined the clinical data of pregnant females who received a routine prenatal examination, Thin Prep cytology test (TCT), and HR-HPV diagnosis during weeks 12–14 of gestation from January 1, 2013, to December 31, 2021, in Beijing Chaoyang Hospital. During the study period, 6285 pregnant females met the primary screening criteria. Specialists made diagnoses based on TCT and HR-HPV results, and obstetricians, pediatricians, cervical pathologists and pathologists jointly performed anticipatory monitoring and obstetric management.

Part II

Inclusion criteria: Pregnant females registered in Beijing Chaoyang Hospital underwent TCT and HPV tests during weeks 12–14 of gestation, then received antenatal care and gave birth in Beijing Chaoyang Hospital. Medical data and basic characteristics were recorded, including menstrual and reproductive status, family history, cervical screening, and obstetric outcomes, including maternal and neonatal complications and comorbidities.

Exclusion criteria: We excluded incomplete or missing cases, females with a history of chronic inflammatory disease or taking long-term immunosuppressive medication, females with a history of chronic diseases, females with human immunodeficiency virus infection, females with induced abortions due to fetal malformation or other personal reasons, or females with a history of cervical surgical treatment or multiple pregnancies (twins or more).

Study endpoint: The primary endpoint was the pregnancy outcome 3 days after vaginal delivery or cesarean section (CS). The main outcome was HR-HPV infection. Other baseline and obstetric factors included age, gravidity, parity, number of abortions, body weight and height, gestational age at delivery, birth weight of the neonate, and delivery mode. Body mass index (BMI) was defined as the individual's body weight in kilograms divided by their height in meters squared.

Fig. 1 shows the flow chart of the study population. According to the exclusion criteria, 3645 incomplete or missing cases, 238 cases with a history of chronic diseases, 198 cases with a history of chronic inflammatory disease or taking long-term immunosuppressive medication, 147 cases with induced abortions due to fetal malformation or other personal reasons, 68 cases with a history of cervical surgical treatment, and 173 multiple pregnancies (twins or more) were deleted. There were 1816 pregnant females (414 HR-HPV positive and 1402 HR-HPV negative) assessed for eligibility.

Through a nearest-neighbor propensity score matching (PSM), we matched HR-HPV-positive and HR-HPV-negative pregnant women using caliper width equal to 0.02. One-to-one PSM was applied to all of the pregnant women's clinical features, such as age and pre-pregnancy BMI, to achieve a standardized difference of less than 0.15. After PSM, 171 HR-HPV-positive and 171 HR-HPV-negative pregnant females were included in the study, in order to analyze the association between HR-HPV infection and maternal-fetal pregnancy outcomes.

HPV Genotyping

The HPV genotypes were identified using the HR-HPV Type Nucleic Acid Detection Kit (Shanghai Zhijiang Biotechnology Co., Ltd., Shanghai, China). Using this kit, 13 types of HPV-specific DNA segments were distinguished with the aid of the TaqMan process via the corresponding 13 types of HPV-specific primers and fluorescent probes. This test individually identified 13 HR-HPV subtypes, including HPV-16, HPV-18, HPV-31, HPV-33, HPV-35, HPV-39, HPV-45, HPV-51, HPV-52, HPV-56, HPV-58, HPV-59, and HPV-68.

Adverse Pregnancy Outcomes

The adverse pregnancy outcomes were defined as follows:

• Spontaneous abortion was characterized as a natural loss of the products of conception and termination of pregnancy before 20 weeks of gestation.

• Preterm delivery was defined as childbirth occurring prior to the 37th week of pregnancy.

• Premature rupture of membranes (PROM) was defined as rupture of the chorioamniotic membranes before the initiation of labor.

• Preeclampsia was defined as systolic blood pressure $\geq$140 mmHg and/or diastolic blood pressure $\geq$90 mmHg on two or more occasions, and measured 4 hours apart in

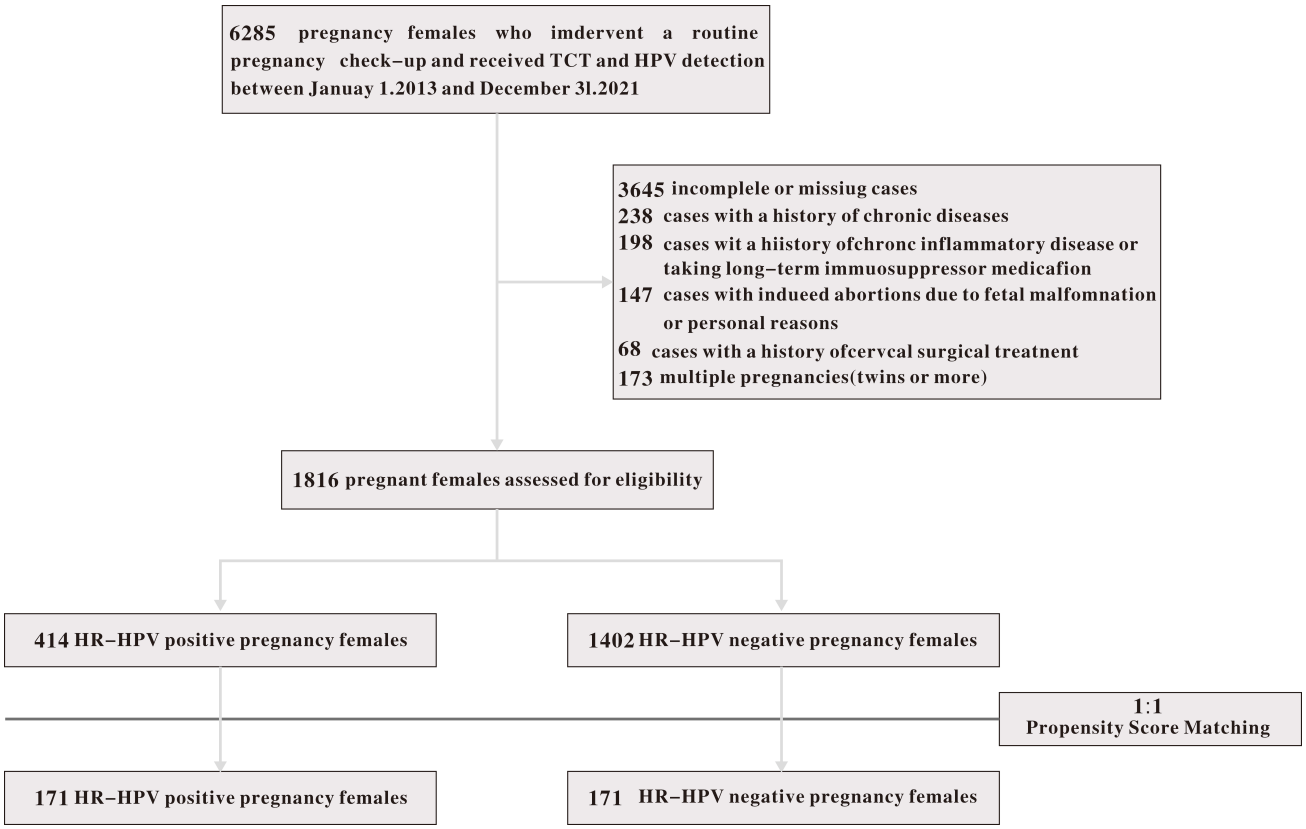

Fig. 1. The flow chart of the study population. The figure was drawn with Microsoft Visio version 2019 (Microsoft Corp., Redmond, WA, USA). TCT, Thin Prep cytology test; HPV, human papillomavirus; HR-HPV, high-risk HPV.

previously normotensive females, along with one or more of the following new-onset conditions at or post-20 gestational weeks: evidence of other maternal organ dysfunction, proteinuria, and uteroplacental dysfunction.

• Oligohydramnios was defined as amniotic fluid index (AFI) $\leq$5 cm or the absence of a pocket measuring at least 2 $\times$ 1 cm.

• Fetal growth restriction was defined as an estimated fetal weight below the 10th percentile for gestational age.

• Placenta previa was defined as an abnormal placenta overlying the endocervical os.

• Postpartum hemorrhage was defined as blood loss $\geq$500 mL after delivery within 24 hours.

Statistical Analyses

Statistical analyses in this study were conducted using SPSS, 25.0 software (SPSS Inc., Chicago, IL, USA). We evaluated the distribution of continuous variables for normality employing the Kolmogorov–Smirnov test for sample sizes greater than 2000 and the Shapiro–Wilk test for sample sizes of 2000 or fewer. Continuous variables were expressed as mean values with standard deviations, or the median and interquartile range, as appropriate. Categorical variables were denoted as percentages. We explored the differences between categories in relation to HR-HPV using the Student's *t*-test for normally distributed continuous variables and the Mann–Whitney U test for variables with skewed distributions. Categorical variables were analyzed by employing the Chi-square test or Fisher's exact test, as appropriate. The significance of results was determined using nominal, two-tailed p values, with a threshold of $p < 0.05$ indicating statistical significance.

Results

Prevalence of HR-HPV

In preliminary analysis, 737 pregnant females were HR-HPV positive (overall positive rate, 11.73%). Fig. 2 shows the HR-HPV infection rate during the nine years, varying from 10.31% to 15.45%. The study data reflected that single-genotype infection was more prevalent than multiple-genotype infection (585/737 [79.38%] vs. 152/737 [20.62%]). Of the pregnant females with multiple-genotype infections, 116 were infected with two types of HR-HPV, 32 with three types of HR-HPV, and 4 with four or more types of HR-HPV.

Features of the HPV infection and its distribution across various age categories are depicted in Table 1. The difference in HR-HPV infection prevalence across the four age categories (<25 years, 25–29 years, 30–34 years, and $\geq$35 years) was significant (χ^2 = 10.054, p = 0.018). The <25 years age category demonstrated the high-

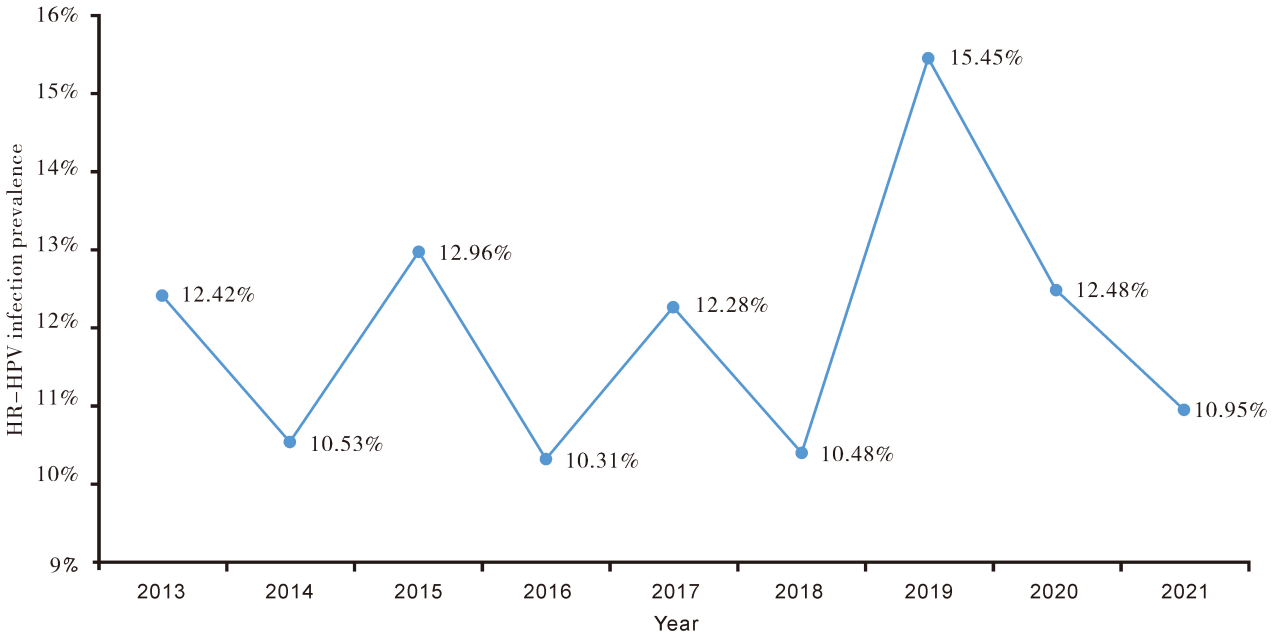

Fig. 2. HR-HPV infection rate over the 8-year period from 2013 to 2021. The figure was conducted using Microsoft Office 2016 Excel software (Microsoft Corp., Redmond, WA, USA).

Table 1. Single and multiple-type HPV infections at different ages.

Age (years)	N	HPV positive	Single-type infection	Multiple-type infection
		n (%)	n (%)	n (%)
<25	217	39 (17.97)	27 (12.44)	12 (5.53)
25–29	2582	285 (11.04)	230 (8.91)	55 (2.13)
30–34	2737	318 (11.62)	260 (9.50)	58 (2.12)
≥35	749	95 (12.68)	68 (9.08)	27 (3.60)

est prevalence of HR-HPV (39/217, 17.97%), whereas the 25–29 years age category exhibited the lowest prevalence (285/2582, 11.04%) (Table 1). Fig. 3 depicts the age distribution of HPV infection prevalence. The age-specific HPV prevalence displayed a "U-shaped" curve indicating a dual peak of HPV infection. The initial peak was observed among pregnant women aged <25 years, followed by a rapid decline. The second peak was observed in females in the ≥35 years category. Moreover, multiple-genotype infections were more prevalent in younger women than in older women.

HR-HPV Genotype Distribution

The five most prevalent HR-HPV genotypes in the current study were HPV-52, HPV-58, HPV-16, HPV-51, and HPV-39, exhibiting frequencies of 2.90%, 2%, 1.94%, 1.38%, and 1.29%, respectively, regardless of the status of single-genotype or multiple-genotype infections (Fig. 4).

The HR-HPV genotype distribution also varied according to age category (Fig. 5). The five most prevalent HR-HPV genotypes in the <25 years category were HPV-52 (4.6%), HPV-58 (4.1%), HPV-51 (3.7%), HPV-16 (2.3%), and HPV-39 (2.3%). The five most common HR-HPV genotypes in the 25–29 years category were HPV-52 (2.6%), HPV-16 (2.0%), HPV-58 (1.8%), HPV-51 (1.5%), and HPV-39 (1.2%). For the 30–34 years category, the five most common HR-HPV genotypes were HPV-52 (2.8%), HPV-58 (1.9%), HPV-16 (1.8%), HPV-39 (1.2%), and HPV-56 (1.2%). Lastly, the five most common HR-HPV genotypes in the ≥35 years category were HPV-52 (3.7%), HPV-58 (2.4%), HPV-16 (2.1%), HPV-39 (1.6%), and HPV-51 (1.3%).

Relationship between HR-HPV and Maternal-Fetal Pregnancy Outcomes

According to the inclusion criteria and exclusion criteria, there were 1816 pregnant females assessed for eligibility.

The basic characteristics of the enrolled pregnant females before and after PSM are summarized in Table 2. Before PSM, 414 HR-HPV-positive pregnant females and 1402 HR-HPV-negative pregnant females were enrolled in the study. As for the clinical features, the mean maternal age (30.5 vs. 30 years) and pre-pregnancy BMI (21.33 vs.

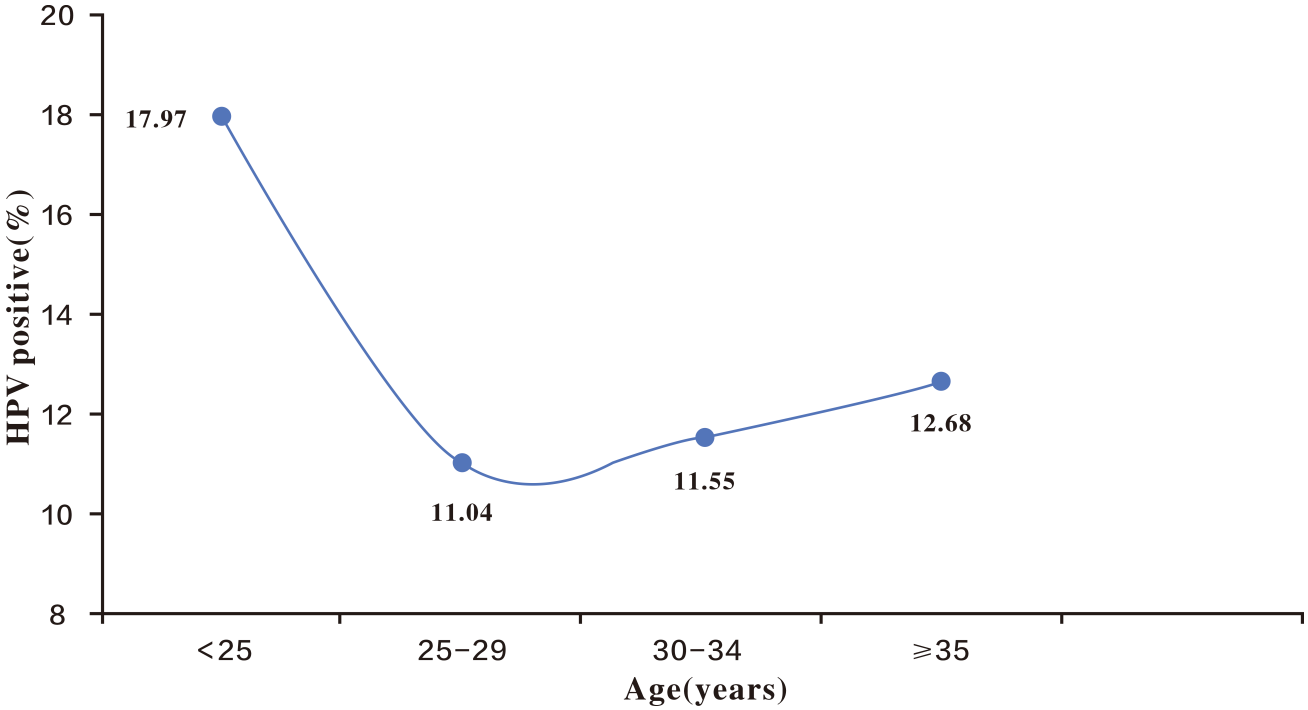

Fig. 3. Age-specific prevalence of HR-HPV. The figure was conducted using Microsoft Office 2016 Excel software (Microsoft Corp., Redmond, WA, USA).

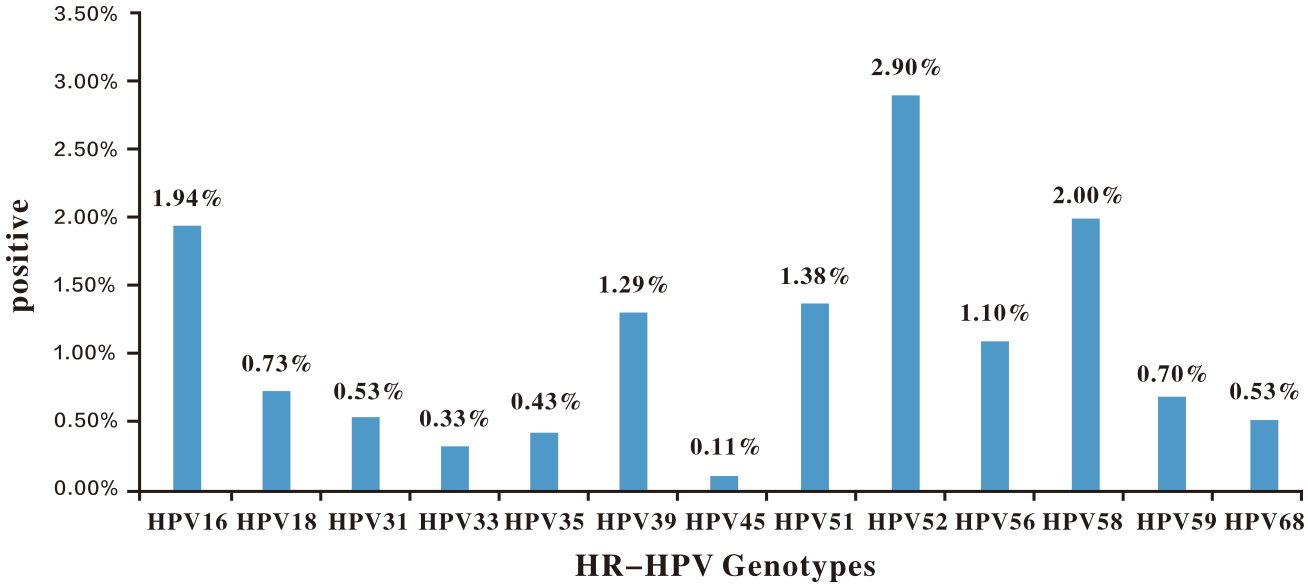

Fig. 4. Distribution of HR-HPV Genotypes. The figure was conducted using Microsoft Office 2016 Excel software (Microsoft Corp., Redmond, WA, USA).

20.9 kg/m^2) were higher in the HR-HPV-negative pregnant women ($p < 0.05$). Other clinical features, including gestational age at delivery, gravidity, parity, and number of abortions were not significantly different between groups (Table 2). After PSM, 171 HR-HPV-positive pregnant women and 171 HR-HPV-negative pregnant women were included in the study. The clinical features were well-balanced between the two groups (Table 2).

Table 3 compares the maternal-fetal pregnancy outcomes between the two groups. Our study found no significant difference between the two groups in the following maternal-fetal pregnancy outcomes: spontaneous abortion (1.2% for HR-HPV positive, 0% for HR-HPV negative, $p = 0.478$), preterm delivery (4.7% for HR-HPV positive, 5.3% for HR-HPV negative, $p = 0.804$), premature rupture of membrane (28.8% for HR-HPV positive, 22.8% for HR-HPV negative, $p = 0.216$), preeclampsia (7.6% for HR-HPV

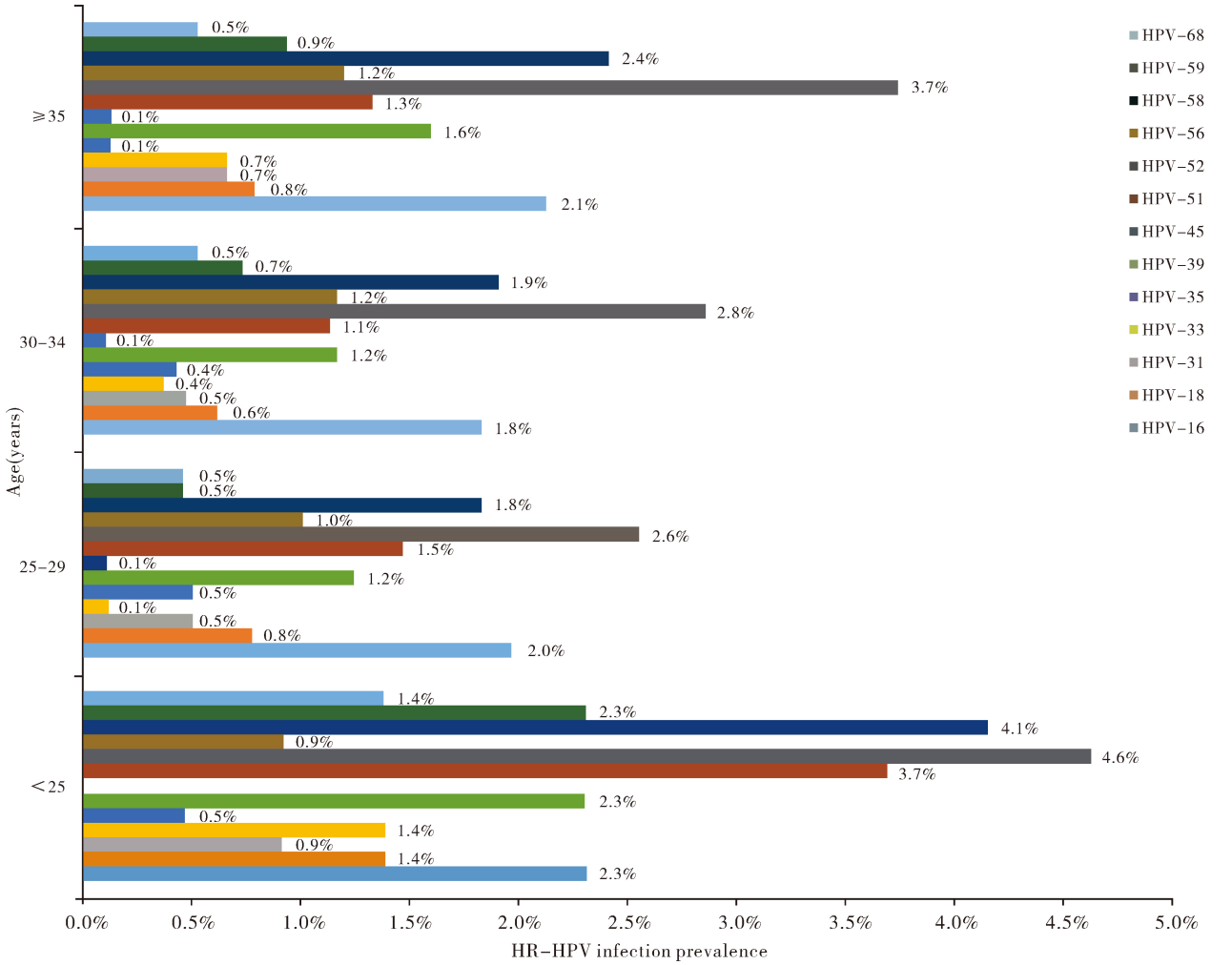

Fig. 5. HR-HPV genotype distributions of different age groups. The figure was conducted using Microsoft Office 2016 Excel software (Microsoft Corp., Redmond, WA, USA).

positive, 7.6% for HR-HPV negative, $p = 1$), oligohydramnios (8.2% for HR-HPV positive, 7% for HR-HPV negative, $p = 0.683$), fetal growth restriction (1.8% for HR-HPV positive, 0.6% for HPV negative, $p = 0.615$), placenta previa (1.2% for HR-HPV positive, 0.6% for HR-HPV negative, $p = 1$), postpartum hemorrhage (8.9% for HR-HPV positive, 11.2% for HR-HPV negative, $p = 0.47$) (Table 3). There was also no significant difference in delivery mode or birth weight between the two groups (Table 3).

Discussion

Studies indicate that the prevalence of HR-HPV in the general population of China is 13.3–18.4%; however, it is 5.4–37.2% for gestating females [5]. Previous study has revealed that the incidence of HR-HPV infection in gestating females is elevated compared to that in non-gestating females, owing to the immunosuppressive role of hormones [16]. Elevated levels of steroid hormones repress cell-regulated immunity, which is essential for clearing HPV infections. It has been suggested that HPV infection is facilitated by the modified immunological adaptations, which are aimed at maintaining immune tolerance towards the semi-allogeneic fetus [14]. However, certain studies reported no variation in the rate of HR-HPV infection between gestating and non-gestating females [4,17]. The HR-HPV-positive rate in gestating females in the current study was 11.73%, comparable to the 12.5% reported by Takakuwa *et al*. [18] in 1183 pregnant females. Furthermore, they established no significant difference in their study in the HR-HPV-positive rate between gestating and non-gestating females (12.5% vs. 12.8%) [4,18]. Our study showed that the HR-HPV-positive rate in pregnant females during the nine study years varied from 10.31% to 15.45%. Another study from the Beijing Chaoyang Hospital in 2015 revealed that the incidence of HR-HPV infection in the hospital opportunistic screening population was 10.4% [19]. Moreover, HR-HPV infections were significantly age-specific among pregnant females, which corroborated the findings of other studies. Takakuwa *et al*. [18] reported that the incidence of HR-

Table 2. The basic characteristics of the pregnant females in Part II.

Clinical features	Before PSM				After PSM			
	HR-HPV positive (N = 414)	HR-HPV negative (N = 1402)	χ^2/Z value	*p* value	HR-HPV positive (N = 171)	HR-HPV negative (N = 171)	χ^2/Z value	*p* value
Maternal age (years)	30.00 (27.0–33.0)	30.50 (28.0–33.0)	–2.608	0.009	30 (28–32)	30 (28–32)	0.000	1.000
Pre-pregnancy BMI (kg/m^2)	20.90 (19.33–22.84)	21.33 (19.59–23.55)	–2.637	0.008	20.8 (19.6–22.04)	20.80 (19.59–22.04)	–0.001	0.999
Gestational age at delivery (weeks)	39 (38–40)	39 (38–40)	–0.502	0.615	39 (38–40)	39 (38–40)	–1.491	0.136
Gravidity			0.703	0.402			1.191	0.275
Primigravida n (%)	247 (59.66)	804 (57.35)			102 (59.65)	92 (53.80)		
Multigravida n (%)	167 (40.34)	598 (42.65)			69 (40.35)	79 (46.20)		
Number of abortion			4.282	0.233			0.593	0.898
0 n (%)	284 (68.60)	938 (66.90)			115 (67.25)	110 (64.33)		
1 n (%)	85 (20.53)	329 (23.47)			34 (19.88)	39 (22.81)		
2 n (%)	38 (9.18)	99 (7.06)			17 (9.94)	18 (10.53)		
≥3 n (%)	7 (1.69)	36 (2.57)			5 (2.92)	4 (2.34)		
Parity			2.014	0.156			0.019	0.889
Primipara n (%)	344 (83.09)	1121 (79.96)			139 (81.29)	140 (81.87)		
Multipara n (%)	70 (16.91)	281 (20.04)			32 (18.71)	31 (18.13)		

Continuous variables are presented as medians with ranges, categorical variables are presented as numbers with percentages.

BMI, body mass index; PSM, propensity score matching.

Table 3. Association between HR-HPV infection and maternal-fetal pregnancy outcomes.

Maternal-fetal pregnancy outcomes	HR-HPV positive (N = 171)	HR-HPV negative (N = 171)	χ^2/Z value	*p* value
Spontaneous abortion n (%)	2 (1.2)	0 (0)	0.503	0.478
Preterm delivery n (%)	8 (4.7)	9 (5.3)	0.062	0.804
Premature rupture of membranes n (%)	49 (28.8)	39 (22.8)	1.530	0.216
Preeclampsia n (%)	13 (7.6)	13 (7.6)	0.000	1.000
Oligohydramnios n (%)	14 (8.2)	12 (7)	0.167	0.683
Fetal growth restriction n (%)	3 (1.8)	1 (0.6)	0.253	0.615
Placenta previa n (%)	2 (1.2)	1 (0.6)	0.000	1.000
Postpartum hemorrhage n (%)	15 (8.9)	19 (11.2)	0.523	0.470
Delivery mode				
Cesarean section n (%)	78 (45.6)	69 (40.4)	0.966	0.326
Vaginal delivery n (%)	93 (54.4)	102 (59.6)	0.966	0.326
Birth weight (g)	3350 (3120–3590)	3350 (3067–3610)	–0.572	0.567

HPV infection among gestating females in the <25 years category was significantly elevated compared to that of women in the >25 years category, and the identical pattern was observed in non-gestating females as well. This could be attributed to the increased frequency of sexual activity or multiple sexual partners in the younger age category when compared to the older category [4]. Our study has detected a double peak of HR-HPV infection in pregnant females, as observed in the general population [20–22]. The first peak was observed for pregnant females in the <25 years category and the second peak was for those in the ≥35 years category. For the present study, the overall HPV infection rate in the youngest age category (aged <25 years, 17.97%) was relatively elevated compared to other age categories. This was followed by a sharp decline in the rate of HR-HPV infection in the older age groups. The higher infection rate in the youngest age group may be related to more frequent sexual activities and a relatively inadequate immune response. As for the second peak, one explanation could be alterations in the sexual attitudes of females of this age category and their partners [4]. Another reason could be that most women get pregnant within a restricted age bracket. Only a small percentage of females become pregnant after 40 years of age. This study demonstrated that multiple-genotype infections were more common among younger women. This finding corroborated prior research findings and could be explained by increased sexual activity among younger females, which leads to the sexual transmission of multiple HPV genotypes [23].

The geographical prevalence of HPV genotypes has been widely explored in the literature, and prevalence patterns have been identified [24,25]. HPV-16 and HPV-18 are reportedly prevalent globally, whereas HPV-52 and HPV-58 are more common in Asia [23]. The WHO data indicate that the five most frequent HPV types in Chinese females with CC are HPV-16, HPV-18, HPV-58, HPV-33, and HPV-52. On the other hand, those most common in the general Chinese female population are HPV-16, HPV-52, HPV-51, and HPV-58 [20,25,26]. The present study established that HPV-52, HPV-58, HPV-16, HPV-51, and HPV-39 were the five predominant genotypes among the pregnant females in the study, corroborating the findings of previous Chinese research [26,27]. Surprisingly, HPV-18 was only the 7th most prevalent genotype in the study group, whereas it is reportedly very common in Western females. At present, three licensed HPV vaccines are available, including bivalent (HPV-16 and HPV-18), quadrivalent (HPV-6, HPV-11, HPV-16, and HPV-18), and nonavalent (HPV-6, HPV-11, HPV-16, HPV-18, HPV-31, HPV-33, HPV-45, HPV-52, and HPV-58) vaccines in mainland China. The bivalent, quadrivalent, and nonavalent vaccines were launched and approved for application by the China Food and Drug Administration in 2016, 2017, and 2018, respectively [20,28]. However, these commercial vaccines only confer protection against a few genotypes, as per epidemiological data from Western countries [20,28]. More studies and data focused on the epidemiological aspects of HR-HPV in China are urgently needed.

Infectious pathogens during gestation have repeatedly been linked to adverse pregnancy outcomes and severe neonatal sequelae [8,14]. The contribution of HR-HPV in the progression and outcomes of pregnancy is not yet well understood [14]. Moreover, discrepancies are present in the existing literature on the association of HR-HPV with adverse pregnancy outcomes. Some studies have demonstrated no relationship between HR-HPV infection and adverse pregnancy outcomes [8,9,29], whereas others have revealed a link with adverse pregnancy outcomes like preterm birth [30], PROM [6], spontaneous abortion [31], pregnancy-related hypertensive disorders [32], intrauterine growth restriction [13], and death of the fetus [14]. Different types of samples (Pap smear, HPV DNA cervical swab, amniotic fluid, placenta), variable timing of sampling (during pregnancy, post-partum, within 3 years to delivery), and mechanism of action evaluated (cervical lesion, placental and membranes infection) may contribute to the heterogeneous and inconsistent results [33]. A previous study revealed that the major risk factor for preterm delivery was

HPV-related cervical high-grade squamous intraepithelial lesion (HSIL), not HPV infection alone [10,33]. Another review also demonstrated a higher risk for preterm delivery due to HPV infection only for Caucasian women, not for the Asian population [10,34]. It was reported that there are two different pathways in the natural history of HPV infections, such as the infectious virion producing pathway and the clonal transforming pathway [11,35]. HR-HPV usually induces more rapid cell division and develops along the clonal transforming pathway, which leads to cancer [11]. On the other hand, LR-HPV usually develops along the infectious virion producing pathway, which results in early abortion or subfertility [11]. Accordingly, a previous survey showed a significant association between HPV infection and spontaneous abortion; however, when only HR-HPV was included, no association was found [11].

Our research showed no significant differences between HR-HPV-positive and HR-HPV-negative pregnant females in maternal-fetal pregnancy outcomes including spontaneous abortion, preterm delivery, premature rupture of membrane, preeclampsia, oligohydramnios, fetal growth restriction, placenta previa, and postpartum hemorrhage. There was also no significant difference in delivery mode or birth weight between the two groups.

Almost 80% of HPV cases in the general population resolve spontaneously within a year or two. Nevertheless, increasing evidence indicates that HPV is more likely to persist during gestation and regress following delivery [7,32,36,37]. Furthermore, the elevation in steroid hormones during gestation can alter the immune system of the mother and enhance fetal "tolerance" but reduce the ability to eliminate infections like HPV [32,38]. Hence, considering the slow clearance rate of HPV combined with the increased vulnerability to HPV due to gestational hormones, it is crucial to consider the timing of HPV diagnosis and the necessity for repeated screenings. We will explore the progression of HR-HPV infection during gestation and following delivery in future studies.

This research provides a thorough evaluation of the features of HR-HPV infection in pregnant females in Beijing. However, it has several limitations. Firstly, this was a hospital-based survey study and it did not include data from the general population during the same period. Secondly, the rate of loss to follow-up was high and the results might be biased. Thirdly, the lack of information regarding socioeconomic status and sexual behaviors makes it difficult to provide practical guidance for HPV infection prevention.

Conclusions

HPV-52, 58, and 16 were the most prevalent HPV genotypes in pregnant females. This study showed no significant differences in maternal-fetal pregnancy outcomes between HR-HPV-positive and HR-HPV-negative groups. Previous studies in this area have reached conflicting conclusions. More studies are needed to elucidate the effect of HR-HPV infection on maternal-fetal pregnancy outcomes. Moreover, the infection persistence and clearance rates are not well understood. Additional follow-up studies are needed to guide the treatment of HR-HPV infection during pregnancy.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

SW participated in the design and coordination of the study. YL performed the data acquisition, statistical analysis and drafted the manuscript. Both authors have been involved in drafting the manuscript and revising the manuscript critically. Both authors have read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

During the study, all participants were informed of the potential use of their data for future research. The study was approved by the human ethics committees of the Beijing Chaoyang Hospital and the Capital Medical University. The full name is study on the prediction model of cervical low-grade intraepithelial neoplasia progressing to high-grade lesions. The ethics batch number is 2023-6-29-1. Because of the retrospective nature of the study, written informed consent was exempted by the human ethics committees of the Beijing Chaoyang Hospital and the Capital Medical University.

Acknowledgment

We thank all the medical staff of Beijing Chaoyang Hospital and the Capital Medical University for their support in the study. We thank all the patients recruited in the study. We appreciate the linguistic support provided by Zhiyun for the study.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

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