

Analysis of age-specified prevalence and multiple HPV-type prevalence in a Chinese population

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Abstract

Background: The human papillomavirus (HPV) is one of the most widespread viruses on the planet. A previous study found that HPV prevalence has an age-related relationship. Multiple HPV infections have a bad outcome. HPV infection is linked to uterine cervical cancer, bacterial vaginitis, cervicitis, fungal vaginitis, and pelvic inflammation, among other gynecological conditions. Furthermore, HPV infection during pregnancy has a negative impact on the health of both the mother and the fetus. In Chinese women, the prevalence of HPV and the link between HPV infection and various diseases are still unknown.

Methods: A Genotyping Test Kit was used to determine individual HPV genotypes (Life River Co., Shanghai, China). The prevalence of HPV types and ages was collected and analyzed by using SPSS 22.0 software.

Results: The HPV infection positive rate was 20.3% overall, including HPV single genotype (74.3%), HPV double genotype (18.4%), and HPV triple infections (7.4%). The top fifth prevalent HPV genotypes were HPV52 (25.5% of the positive individuals), HPV16 (19.7%), HPV58 (21.7%), HPV51 (11.4%) and HPV39 (9.6%). The <20-year old group represented highest HPV infection rate, and HPV infection rates rise with age, especially multiple HPV infection rates. There were significant differences for fungal vaginitis ($P=0.010$; $\chi^2=6.61$) and cervical lesions ($P=0.000$; $\chi^2=1069.60$) with the health check group. The prevalence of HPV infection is significant popular among fungal vaginitis ($P=0.010$; $\chi^2=6.61$) and cervical lesions ($P=0.000$; $\chi^2=1069.60$). The early pregnant women, middle-late pregnant women HPV positive ration was lower than routine health checks HPV infection rates. hpv52: hpv58 enjoy the highest infection rate among the multiple HPV combination.

Conclusion: HPV infection was serious among women in China. HPV infection is linked to one's age in Chinese. Women under the age of 20 have the highest HPV prevalence, implying that HPV vaccination is required for young people. Multiple HPV infections have a cumulative effect as people become older. It's possible that HPV infection is linked to vaginitis since vaginitis makes you more susceptible to infection. HPV infections in pregnant women are common and require additional care.

Introduction

Human papillomavirus (HPV) is one of the most common viruses worldwide[1]. The papillomavirus was first found in rabbit "long horned", and later, papillomavirus infections were found to exist in widely species, including humans[2]. HPV infection is closely linked with sexual activity and age in human, begins at the earliest ages of sexual activity [3]. Perivenous study showed most HPV infections are cleared spontaneously within two years after infection [4], the HPV infection risk relatively stable when approximately 30 years old[5]. But it's not clearly the HPV prevalence in different Chinese ages.

HPV infection is closely related to various gynecological diseases. HPV infection is considered to be the culprit of cervical cancer [6]. Virus infection is correlated with bacterial vaginitis and fungal vaginitis, and also, virus invading affects the richness and diversity of vaginal flora[7]. Cervicitis is general considered pathogenic by mycoplasma, and HPV is supposed to potential pathogen[8]. pelvic inflammation is common and harmful gynecological diseases, HPV probably play significant role in this pathema. Besides, HPV infection is supposed to interrelated to prematurity, spontaneous abortions and other perinatal complications[9]. In conclusion, it is worthy analyzing the prevalence of HPV among common gynecological diseases in Chinese.

The virus is a semi organism, which uses the host cell device to accomplish replication and reproduction. HPV invade the host cell, size host cells by holding biological activities, inhabiting cell apoptosis, inducing abnormal cell cycle and excessive proliferation, case cervical epithelium inflammatory reaction, immune imbalance and cervical carcinogenesis [10]. More than 200 kinds of human papillomaviruses have been identified up to now. Previous study shows that diverse HPV genotypes possessed infection portability[11]. HPV16, HPV18, HPV31, HPV33, HPV39, HPV45, HPV51, HPV52, HPV56, HPV58, HPV59, HPV68 and HPV 82 are the most prevalent HPV types that cause cervical cancer, classified as high-risk HPV

[12]; HPV6 and HPV11 are the most prevalent HPV types that cause benign hyperplasia of cervical lesions classified as low-risk HPV [13].

Multiple infections account for large proportion of HPV-positive individuals, which are closely related to cervical lesions and other gynecological diseases. In the cell entry of virus, may be one cervical cell suffering from various genotypes HPV, or various virus invading diverse cells, altogether various combinations of HPV genotypes shuttling the virus around the cells[14].

To establish a foundation for HPV-based infections, this paper collected and analyzed the information of HPV screening individuals in the Shandong Maternal and Child Health Hospital. We analyzed HPV prevalence on different ages, among five common gynecological diseases and pregnant women, obtaining tips on HPV prevalence in Chinese for follow-up research.

Methods

Ethics Statement

The research was approved by the Ethics Committee of Shandong Maternal and Child Health Hospital Affiliated Shandong University, in accordance with the China Ethical Principles for Biomedical Research Involving Human Subjects and the Declaration of Helsinki for Human Research. The content of the experiment (including the use of tissue samples), the significance of research, and confidentiality of the study have been well informed to the participants, the research was supported by the participants, and informed consent in verbal has been approved by all subjects and/or their legal guardian(s) in case of minors. These procedures of the consents were approved by ethic committee.

Study population and information collection

The study population and information were collected from individuals who sought medical advice in Shandong Maternal and Child Health Hospital from January 2018 to August 2021. Individuals with a basic disease (eg. hypertension, diabetes, dyslipidemia, chronic bronchitis, chronic obstructive pulmonary disease, chronic gastropathy, hereditary diseases, cardiovascular and cerebrovascular diseases, etc.) were excluded; Individuals with cervical cancer or those undergoing cervical surgery were also excluded. Diagnoses of bacterial vaginitis, cervicitis, cervical lesions, fungal vaginitis and pelvic inflammation were based on bacterial cultures and ultrasonic diagnosis results and exactly in accordance with the disease diagnosis guidelines. People in the control groups were selected from the healthy individuals who underwent HPV health checks.

A total of 16525 individuals were included in this study. After eliminating individuals with incomplete information, 13972 individuals were retained, including 2535 low-risk and high-risk individuals undergoing HPV screening, 11437 high-risk individuals undergoing HPV screening, and 39 low-risk individuals undergoing HPV screening. The enrolled individuals were aged from 15 to 83 years.

The flow chart of HPV prevalence analysis is represented in Figure.1.

HPV genotyping

The test samples were obtained from epithelial cells on the surface of the cervix, which was scraped with a specialized cervical brush, and the cells were preserved in a specific cell preservation solution (Life River Co., Shanghai, China). HPV detection and genotyping were performed using an HPV Genotyping Test Kit (Life River Co., Shanghai, China). The kit was used to detect and genotype fifteen high-risk HPV genotypes (HPV16, HPV18, HPV31, HPV33, HPV35, HPV39, HPV45, HPV51, HPV52, HPV56, HPV58, HPV59, HPV66, HPV68, and HPV82) and two low-risk HPV genotypes (HPV6/HPV11).

The experimental steps followed the kit instructions. 1 ml scrape suspension was centrifuged at 13000 rpm, the supernatant was removed, and the precipitate was treated with 100 μ l of cell lysate (from the kit). The precipitate was shaken and boiled

for 10 min. Then, the sample was centrifuged at 13000 rpm, and the supernatant was taken as a template for PCR amplification. PCR mixtures (36 μ l) were mixed with templates (4 μ l) using an ABI7500 instrument for PCR amplification. The PCR procedure was as follows: the mixtures were treated at 50°C for 10 minutes, pre-denatured at 95°C for 10 minutes, denatured at 95°C for 20 seconds, annealed at 60°C for 30 seconds, and then photographed at 60°C for 5 seconds. The procedures were repeated from denaturation to annealing cycles 40. The standard “S” curve was judged to be positive.

HPV type-specific prevalence

According to the infection genotype, the positive individuals were divided into single HPV genotype infection, double HPV genotype infection and triple genotype infection groups. The data were statistically analyzed using SPSS 22.0 software (SPSS Inc., Chicago, IL, USA). Any differences between the groups in prevalence were assessed by chi-squared (χ^2) tests, and $P < 0.05$ was considered statistically significant.

Age-specific prevalence

The statistical sample was divided into 9 age groups, namely, < 20 years, 21–25 years, 26–30 years, 31–35 years, 36–40 years, 41–50 years, 51–60 years, and > 60 years. The HPV infection prevalence in each group was presented using a bar chart or line chart.

Results

2.1 The prevalence of HPV infection among individuals overall.

There were 2828 HPV positive individuals overall, and the positive rate was 20.3% (Table 1). The HPV single genotype group had 2100 cases, accounting for 74.3% of the positive individuals; the HPV double genotype group had 520 cases, accounting for 18.4% of the positive individuals; and the HPV triple genotype group had 208 cases, accounting for 7.4% of the positive individuals.

In the statistics (Table 1), the top fifth prevalent HPV genotypes were HPV52 (5.1% of the total individuals), HPV16 (3.9%), HPV58 (3.2%), HPV51 (2.2%) and HPV39 (1.9%). The top fifth single infection types were HPV52 (21.0% of the HPV single type individuals), HPV16 (15.9%), HPV58 (12.6%), HPV51 (8.6%) and HPV39 (7.1%); The top fifth double infection types were HPV52 (31.7% of the HPV double types individuals), HPV16 (27.5%), HPV58 (21.7%), HPV51 (15.4%) and HPV39 (15.2%); The top fifth triple infection types were HPV52 (65.4% of the HPV triple types individuals), HPV16 (43.6%), HPV58 (43.6%), HPV51 (35.9%) and HPV39 (35.9%).

2.2 Correlation analysis of HPV prevalence with ages

The HPV infection prevalence in each group was shown in Table 2. There were 467 HPV-positive patients among 21–25 years old, which was the largest age group. The youngest age group present the highest HPV infection rate (40.5% of the age-specified individuals), and single HPV infection attributed the mainly type (22.9%). The age-specific HPV prevalence analysis showed that the overall HPV positive rate decreased before 30 years old, and decreased again after 60 years old (Fig. 2.A). HPV infection types analysis showed that the single HPV infection proportion was stable before 55 years old (Fig. 2.B). The double and triple HPV infection rates increased with age overall (Fig. 2. C and D).

2.3 The relationship between HPV infection and gynecological diseases

Among the tested individuals, we analyzed the HPV prevalence among individuals with common gynecological diseases. Data from individuals got bacterial vaginitis (744 cases), cervicitis (531 cases), cervical lesions (352 cases), fungal vaginitis (268 cases), and pelvic inflammatory disease (184 cases) were sorted and analyzed, and individuals who underwent physical examinations (310 cases) were selected as the reference group. The prevalence of HPV infection is significant

popular among fungal vaginitis ($P = 0.010$; $\chi^2 = 6.61$) and cervical lesions ($P = 0.000$; $\chi^2 = 1069.60$). The infection genotype analysis showed that the prevalence of single HPV infection single fungal vaginitis ($P < 0.001$) and cervical lesions ($P < 0.001$) were significantly popular (Fig. 3. A, B, C and D)

The HPV infection genotypes among the individuals with five common gynecological diseases are presented in Fig. 4. The main HPV genotypes popular among physical examinations group were HPV16 (4.1% of the total individuals in the group), HPV52 (4.0%), HPV58 (3.2%), HPV51 (2.0%) and HPV18 (1.7%); the top fifth prevalent HPV genotypes among individuals with cervicitis were HPV52 (3.7%), HPV16 (2.7%), HPV66 (1.8%), HPV56 (1.4%) and HPV58 (1.4%); the top fifth prevalent HPV genotypes among individuals with pelvic inflammation were HPV52 (6.2%), HPV58 (5.4%), HPV16 (4.6%), HPV31 (2.08%), HPV39 (2.08%) and HPV66 (2.08%); the top fifth prevalent HPV genotypes among individuals with bacterial vaginitis were HPV52 (7.1%), HPV16 (4.7%), HPV58 (4.5%), HPV66 (2.4%), and HPV56 (2.06%); the top fifth prevalent HPV genotypes among individuals with fungal vaginitis were HPV52 (5.8%), HPV58 (4.2%), HPV16 (3.6%) and HPV39 (2.3%); and the top fifth prevalent HPV genotypes among individuals with cervical lesions were HPV52 (9.7%), HPV16 (9.5%), HPV58 (7.3%), HPV66 (4.6%) and HPV56 (3.7%).

2.4 The HPV prevalence among the pregnant women.

To investigate the rate of HPV infections of pregnant women, we analyzed HPV infection of early pregnant women, middle-late pregnant women and abortion women. The quantity of HPV positivity is 82, 492 and 666 sequential. The early pregnant women, middle-late pregnant women HPV positive ration was lower than routine health checks HPV infection rate, especially the triple genotype infection rate (Table 3). The top fifth prevalent genotypes in women with HPV infections were the same as those of the women undergoing routine health checks.

2.5 The prevalence of HPV combinations infection types overall.

To investigate the HPV genotype coupled among multiplied HPV infections individuals, The HPV genotype coupled infected individual was statistically analyzed (Table 4). The most common types of infection were HPV52: HPV58 (65 cases, 4.7% of the total combinations cases); HPV16: HPV52 (60 cases, 4.4%); HPV51: HPV52 (46 cases, 3.4%); HPV16: HPV58 (43 cases, 3.1%); and HPV56: HPV66 (35 cases, 2.6%), of which HPV52 had the highest frequency in combination infections.

Discussion

With the evolution of China's economy and society, the concept of sexual activity and the HPV infection rate has changed. There is limitations evidence on the prevalence of HPV in the Chinese in last decades. The survey on the prevalence of different ages and common gynecological diseases were necessary for HPV vaccination and virus transmission prevention.

This research confirmed that the HPV infection is serious in China. Almost one in five women is infected by HPV in China, single genotype other than multiple HPV infection is the mainly infection manner. The top popular genotypes of HPV infections are HPV52, HPV16, HPV58, which is consistent with Asia, but different from the USA (most common genotype HPV16, HPV68 and HPV39)[15]. Multiple HPV infections is common in Chinese. The types with a high frequency of involvement in HPV multiple infections include HPV52, HPV16 and HPV58, which are consistent with the single HPV infection types[16].

The HPV infection was significantly correlated with age. The HPV prevalence curves showed that young women are vulnerable to HPV infections [17]. This may be due to young women having susceptible cervical epithelial cells [18]. Also, may be, young women infected by HPV have poor awareness of hospital treatment. This indicated that vaccinate women who are less than 20 years old from HPV infection is necessary. The rate of multiple HPV infections gradually increases as age increases. It may due to different ages individuals have different lifestyles and habits[19]. Above all, the immunity of

women cervical tissue decreases with age, such as the immune cells Langerhans cell function exhaustion and quantity reduced, leading single HPV infections transformed into multiple HPV infections[20].

In this study, we found that the HPV infection were significantly correlated with cervical lesions and vaginitis. This may due to vaginal microecological weakened the cervical cell 's immunity and increased its susceptibility to HPV virus invading [21]. Besides, individuals got urethritis, cervicitis and pelvic inflammatory disease was prone to carry-over HPV. HPV infection during the pregnancy has recently received more attention[22]. This paper found that pregnant women have a lower prevalence of HPV, this may because the specific habits during pregnancy [23]. In additions, the pregnant women who got HPV infection may be care more carefully.

The combination hpv52: hpv58, hpv16: hpv52 and hpv51: hpv52 has the highest prevalence, which are consistent with prevalence of single HPV[24]. Previous studies have shown that multiple HPV infections are serious worldwide [25]. Interesting, we found HPV multiple infection rate was significantly higher than the product of two single genotype HPV infection probabilities (for example, the HPV16 infection rate was 0.039, and the HPV52 infection rate was 0.051). According to the mathematical probability calculation formula, the probability of a combined infection of HPV16 and HPV52 is $0.039 \times 0.051 = 0.0020$, which is far lower than actual probability HPV16:HPV52 value of 0.0047.), indicating that the infection events of two single genotype viruses are influence each, one virus infection is conducive to the anther virus infection. Probably, the primary virus infection may destroy the original immune system of cervical epithelial cells and increase the incidence of a secondary virus infection in the multiple HPV infection process[26]. The strategy of HPV multiple infections is instrumental in virus transmission and virus evolution, which may be expiations for HPV succeed survival and reproduction world widely[27].

This study has made several significant discoveries, but it also has certain drawbacks. The sample size for HPV infections is limited. Besides, this is not a cohort cross-sectional study, but rather an outpatient survey, which lacking of consistency. Furthermore, there is a scarcity of direct evidence linking HPV infection to common gynecological diseases. There is a need for more extensive and systematic research. in future.

Conclusion

HPV infection was serious among women in China. HPV infection is linked to one's age in Chinese. Women under the age of 20 have the highest HPV prevalence, implying that HPV vaccination is required for young people. Multiple HPV infections have a cumulative effect as people become older. It's possible that HPV infection is linked to vaginitis since vaginitis makes you more susceptible to infection. HPV infections in pregnant women are common and require additional care.

Abbreviations

HPV
Human papillomavirus.

Declarations

Ethics approval and consent to participate

The research was approved by the Ethics Committee of Shandong Maternal and Child Health Hospital Affiliated Shandong University, in accordance with the China Ethical Principles for Biomedical Research Involving Human Subjects and the Declaration of Helsinki for Human Research. The researches were supported by the participants, and informed consent in verbal has been approved by all subjects and/or their legal guardian(s) in case of minors, and these procedures of the consents were approved by ethic committee.

Consent for publication

Not applicable

Availability of data and materials

The aggregate data supporting findings contained within this manuscript will be shared upon request submitted to the corresponding author.

Competing interests

The authors declare that there were no competing interests.

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Authors' contributions

Xiao-Qian Zhang and Ting-Ting Wang carried out the laboratory detection and drafted the manuscript. Xiao-Qian Zhang and Xiao-Li Qu participated in performed the statistical analysis. Yu-Xia Zhou conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1. Prevalence of the different HPV genotypes among the included individuals.

Sorts Genotypes	HPV positive (ratio)	Single type (ratio)	Double types (ratio)	Triple types (ratio)	Total
HPV 16	542 (19.7%)	331(15.9%)	143 (27.5%)	68 (43.6%)	13933
HPV 18	192 (7.0%)	115 (5.5%)	48 (9.2%)	29 (18.6%)	13933
HPV 31	131 (4.8%)	67 (3.2%)	41 (7.9%)	23 (14.7%)	13933
HPV 33	117 (4.2%)	54 (2.6%)	37 (7.1%)	26 (16.7%)	13933
HPV 35	92 (3.3%)	36 (1.7%)	29 (5.6%)	27 (17.3%)	13933
HPV 39	266 (9.6%)	148 (7.1%)	79 (15.2%)	39 (25.0%)	13933
HPV 45	57 (2.07%)	18 (0.9%)	23 (4.4%)	16 (10.3%)	13933
HPV 51	314 (11.4%)	178 (8.6%)	80 (15.4%)	56 (35.9%)	13933
HPV 52	704 (25.5%)	437(21.0%)	165 (31.7%)	102(65.4%)	13933
HPV 56	220 (8.0%)	106 (5.1%)	71 (13.7%)	43 (27.6%)	13933
HPV 58	443 (16.1%)	262(12.6%)	113 (21.7%)	68 (43.6%)	13933
HPV 59	170 (6.2%)	83 (4.0%)	40 (7.7%)	47 (30.1%)	13933
HPV 66	235 (8.5%)	120 (5.8%)	65 (12.5%)	50(32.05%)	13933
HPV 68	198 (7.2%)	92 (4.4%)	63 (12.1%)	43 (27.6%)	13933
HPV 82	70 (2.5%)	27 (1.3%)	28 (5.4%)	15 (9.6%)	13933
HPV6/11	79 (2.8%)	35 (1.7%)	23 (4.4%)	21 (10.1%)	2573
Total	2828	2100	520	208	13972

The ratio is calculated by (the HPV-genotype s positive individual) divided (the total HPV positive, the single HPV positive individual, double HPV positive individual or triple HPV positive individual) respectively.

Table 2. The age-specific prevalence of the 13972 individuals

Genotypes Age(Y)	HPV positive		Single type		Double types		Triple types		Total (No.)
	(No.	Ratio)	(No.	Ratio)	(No.	Ratio)	(No.	Ratio)	
≤20	53	40.5%	30	22.9%	11	8.4%	12	9.2%	131
21-25	379	26.0%	253	17.3%	89	6.1%	37	2.5%	3824
26-30	608	17.6%	467	13.5%	101	2.9%	40	1.2%	3463
31-35	724	18.9%	554	14.5%	123	3.2%	47	1.2%	1461
36-40	396	19.4%	306	15.0%	70	3.4%	20	1.0%	2039
41-45	218	20.8%	172	16.4%	34	3.2%	12	1.1%	1050
46-50	148	20.6%	113	15.7%	26	3.6%	9	1.3%	719
51-55	135	22.5%	103	17.2%	24	4.0%	8	1.3%	599
56-60	88	24.2%	58	16.0%	19	5.2%	11	3.0%	363
>60	67	25.7%	36	13.8%	21	8.1%	10	3.8%	261
Unknown	12	18.8%	8	12.5%	2	3.1%	2	3.1%	62
Total	2828	20.2%	2100	15.0%	520	3.7%	208	1.5%	13972

The age-specific prevalence are calculated by (the total HPV positive,the single HPV positive individual, double HPV positive individual or triple HPV positive individual) divided (total age-specific people) respectively.

Table 3. HPV prevalence in early, middle-late pregnant and abortion women

HPV infection types	Early	Middle -late	Abortion
HPV positive	14 (17.1%)	96 (19.5%)	158 (23.7%)
Single genotype	11 (13.4%)	82 (16.7%)	116 (17.4%)
Double genotypes	3 (3.7%)	13 (2.6%)	32 (4.8%)
Triple genotypes	0 (0.0%)	1 (0.2%)	10 (1.5%)
HPV52	5 (6.1%)	21 (4.3%)	32 (4.8%)
HPV16	3 (3.7%)	19 (3.9%)	22 (3.3%)
HPV51	2 (2.4%)	11 (2.2%)	23 (3.5%)
HPV39	2 (2.4%)	11 (2.2%)	22 (3.3%)
HPV6/11	0 (0.0%)	3 (0.6%)	3 (0.5%)
Total	82	492	666

The ratio are calculated by (the positive women) divided (the number HPV-checked women under different pregnancy states) respectively.

Table 4. The different HPV genotype combinations among women with HPV infections

HPV-Type Count Type	16	18	31	33	35	39	45	51	52	56	58	59	66	68	82	6+ 11
HPV16	-	16	8	18	13	24	7	25	60	16	43	25	20	19	7	15
HPV18		-	6	7	3	11	6	14	13	10	12	6	9	4	1	13
HPV31			-	4	3	6	2	7	16	5	13	2	7	7	2	2
HPV33				-	3	6	4	7	15	10	3	4	6	8	1	2
HPV35					-	4	2	5	15	6	15	2	12	6	2	1
HPV39						-	5	16	31	10	19	15	11	16	2	6
HPV45							-	3	6	4	5	5	4	3	14	1
HPV51								-	46	16	23	18	16	14	9	8
HPV52									-	29	65	30	34	30	11	12
HPV56										-	18	3	35	14	3	3
HPV58											-	17	21	16	4	8
HPV59												-	6	14	3	4
HPV66													-	9	3	1
HPV68														-	2	2
HPV82															-	1
HPV6/11																-
Total	541	192	131	117	92	266	57	314	704	220	443	190	234	198	70	79

Figures

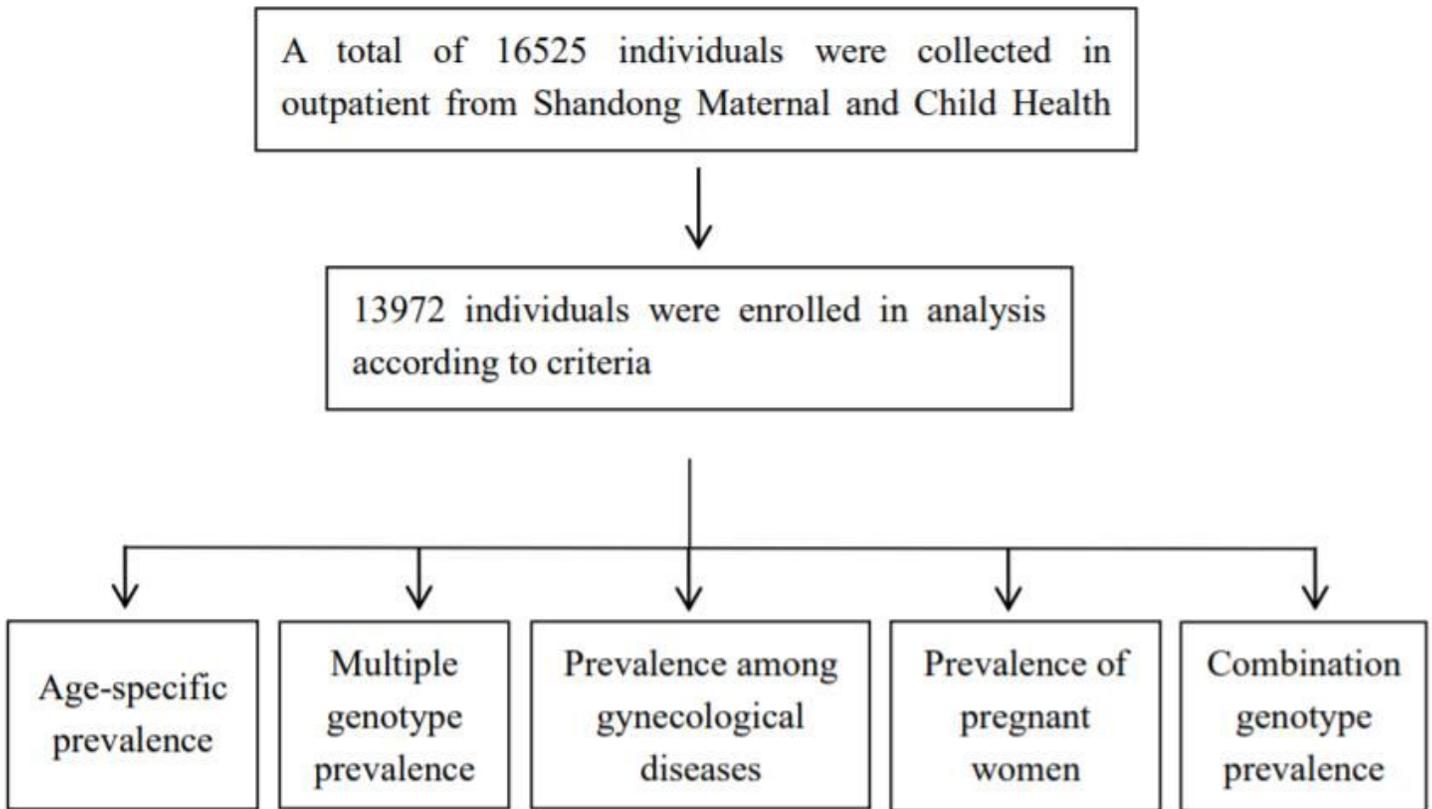


Figure 1

Flow chart of HPV prevalence analysis

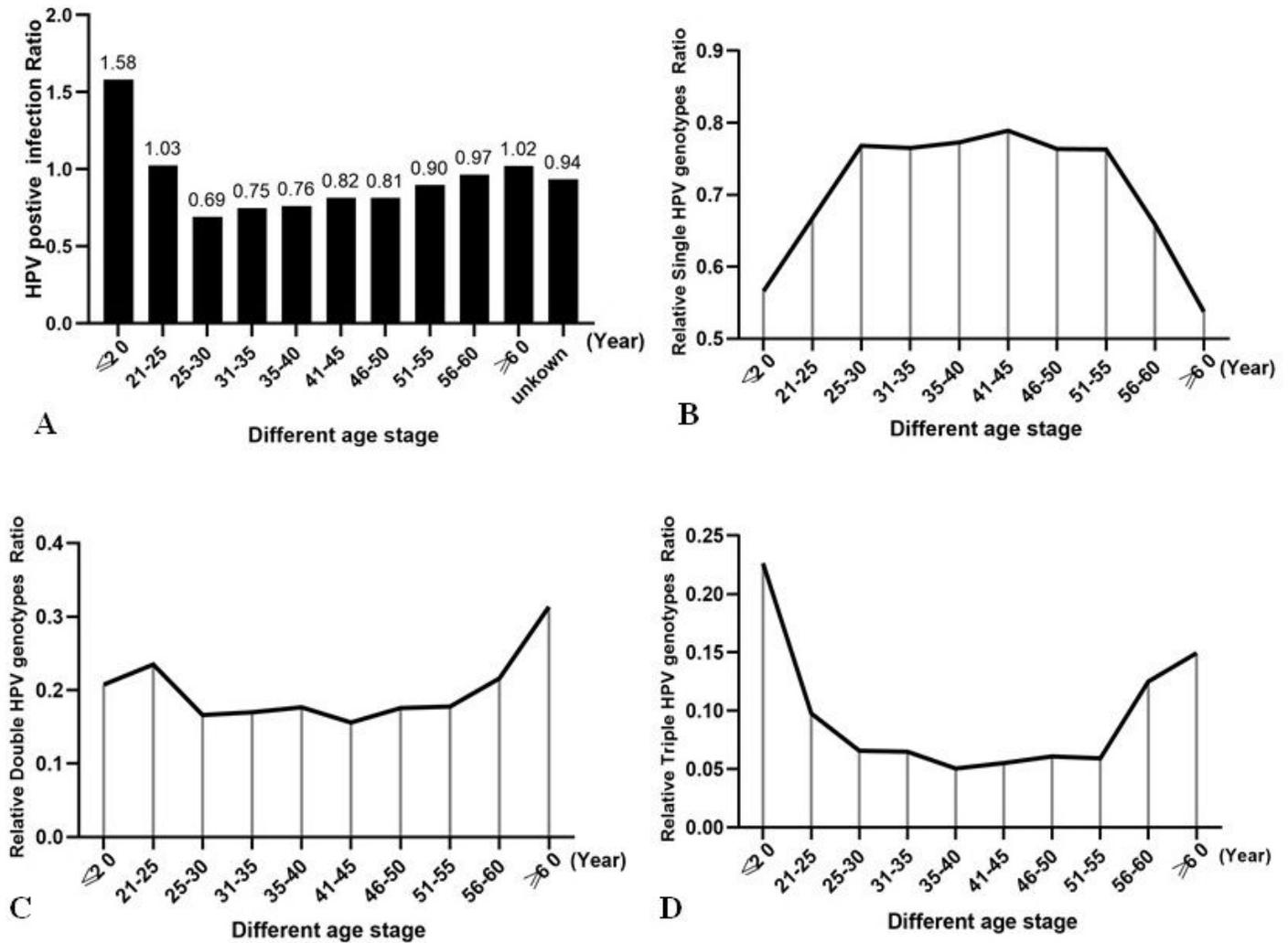


Figure 2

Age-specified HPV prevalence among. A. The overall HPV prevalence at different age stages. B, C and D. The relative single, double and triple HPV genotype ratios at different age stages. HPV-positive infection ratios were calculated by (the HPV-positive individuals)/(total individuals) at different ages, then standardized and presented the data in A. The relative single/double/triple HPV genotype ratios were calculated by (single/double/triple HPV infection ratio)/(HPV-positive infection ratio).

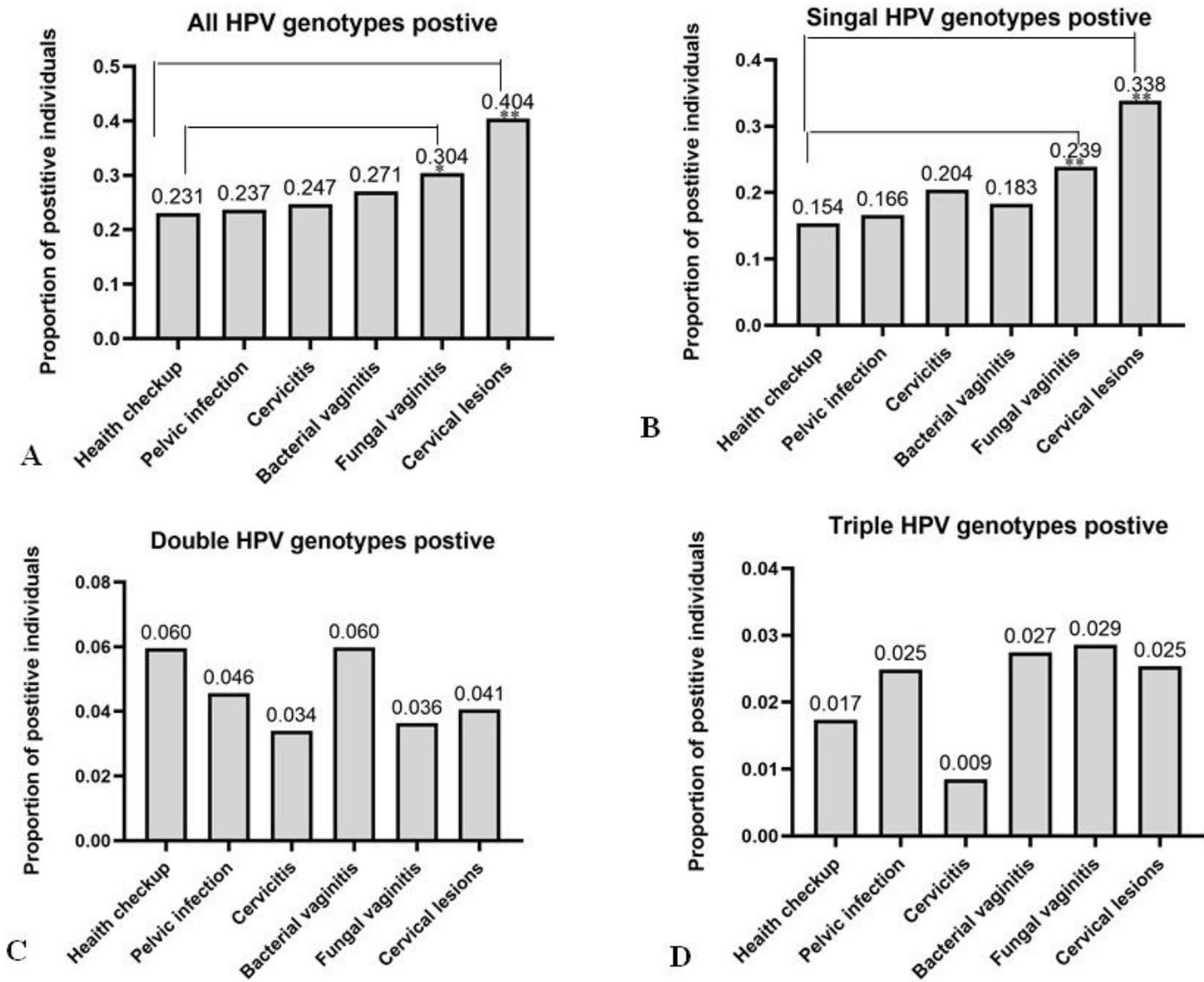


Figure 3

HPV prevalence among people with five common gynecological diseases. A. The overall HPV prevalence among people with five common gynecological diseases. B, C and D. The single, double and triple HPV genotype prevalence among people with five common gynecological diseases.

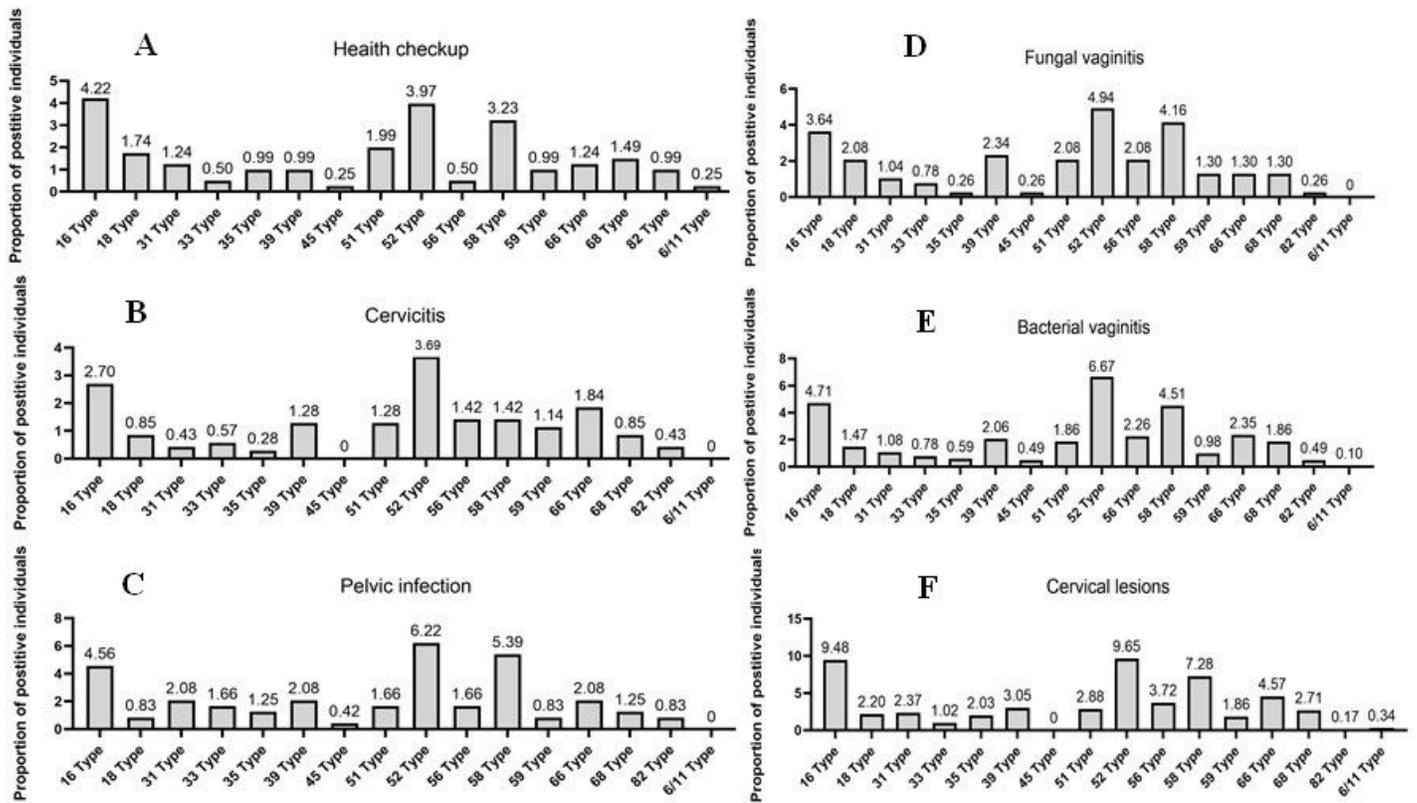


Figure 4

Various HPV genotype infection ratios among individuals with 5 common gynecological diseases. A, B, C, D, E and F represent individuals who underwent routine health checks, with diagnoses of cervicitis, pelvic inflammatory bacterial vaginitis, fungal vaginitis, cervical lesions, and disease, respectively.