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Detecting and genotyping high-risk human papillomavirus among male patients during 2015–2023 in Beijing, China

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ABSTRACT
Few studies focused on human papillomavirus (HPV) in male patients. This study aimed to explore the detection rate and genotyping of HPV among male patients in Beijing to provide a reference for formulating prevention strategies for HPV infection. The cross-sectional study was conducted in Beijing Chaoyang Hospital from November 2015 to March 2023. It covered male patients from the urology and dermatology departments. Fifteen high-risk HPV genotypes were detected by the multiplex real-time polymerase chain reaction method. The overall detection rate of HPV was 25.19% (1288/5114, 95% confidence interval [CI] 24.00%−26.38%), of which the single infection rate was 16.99% (869/5114, 95% CI 15.97%−18.05%) and the co-infection rate was 8.19% (419/5114, 95% CI 7.46%−8.98%). The detection rate of HPV was 40.77% (521/1278), 35.58% (58/163), 32.69% (101/309), 31.91% (60/188), 12.63% (299/2367), and 32.35% (131/405) among male patients with balanitis, warts, rash, urethritis, prostatitis, and other urinary inflammation, respectively ($P < 0.001$). The top five HPV genotypes were HPV-52, HPV-58, HPV-16, HPV-51, and HPV-66. After the first positive HPV test, the proportion of male patients who turned negative was 22.47% within 3 months, 26.40% within 3−6 months, 24.72% within 6−12 months, 17.98% within 12−24 months, and 8.43% more than 24 months. The detection rate of HPV was high among male patients from the urology and dermatology departments in Beijing, which should be considered to develop HPV vaccines with better prevention effects.

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KEYWORDS Human papillomavirus; male; genotype; urology; China

Introduction

Human papillomavirus (HPV) is a group of double-stranded DNA viruses without an icosahedral envelope, which widely exists in nature [1]. More than 200 HPV genotypes have been identified [2,3], which can be divided into low-risk and high-risk genotypes according to their pathogenicity and carcinogenic risk. Low-risk HPV genotypes mainly cause skin warts, including genital condyloma acuminatum and plantar warts. High-risk HPV genotypes can cause mucosal carcinogenesis, and it has been proved that HPV is a direct pathogenic factor for cervical cancer in women [4,5]. The International Agency for Research on Cancer reported 604000 cervical cancer cases and 342000 deaths equivalent to 7.7% of all cancer deaths worldwide in 2020 [6,7]. In the past 30 years, due to the increased awareness of cervical cancer prevention and the popularization of screening, the incidence and mortality of cervical cancer in developed countries have shown a significant downward trend [8]. The incidence of condyloma acuminatum showed a significant upward trend in the 1980s, and in 1990 the number of patients accounted for about 28.6% of the number of sexually transmitted diseases in China. The prevalence of HPV among females in mainland China was 20.6%~31.5% [8], and the HPV detection rate among women diagnosed with cervical intraepithelial neoplasia in Yunnan was over 90% [9].

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HPV infection among male has significantly increased the risk of cervical cancer in their sexual partners [4,10,11]. Although the majority of men with HPV infection were asymptomatic or subclinical cases, HPV still caused malignant diseases such as anal or penile cancer in men [12,13]. Nearly 34,800 new cases of HPV-related cancers were diagnosed in the United States each year, of which 13,100 were in men [14], and up to 50% of penile cancers were estimated to be either directly or indirectly driven by HPV, of which HPV-16 was the most frequently isolated [12]. There was still no drug to eradicate HPV, and the vaccine was the most effective way to reduce HPV [4]. In recent years, a variety of HPV vaccines have been licensed worldwide and widely used in the prevention of HPV [2,15]. In 2017, 71 countries (37%) reported offering HPV vaccines for women compared to 11 (6%) for men [14]. However, HPV vaccines were not recommended for boys mainly owing to little recognition of an emerging epidemic of HPV-associated cancers in men [16].

Current studies on HPV infection among males have mainly focused on high-risk population, such as men who had sex with men or who attended sex clinics, or those who have high-risk sexual behaviours [2,14,16,17]. HPV detection rate was 77.1% among men who had sex with men [18] and 44% among heterosexual and homosexual male attendees of the sexually transmitted diseases clinic in Beijing [16]. Among heterosexual men with HIV positive, the detection rate of HPV was 30.6% in Taizhou, China [17]. The prevalence and genotypes of HPV infection varied by population and geographic regions [19,20]. But, a few studies were conducted on male patients infected with HPV in China.

Therefore, this study aimed to analyse the prevalence and genotypes of HPV infection among male patients in Beijing to provide scientific evidence for HPV prevention and vaccine development.

Material and methods

Study site

This study was conducted in Beijing Chaoyang Hospital affiliated to Capital Medical University, which was a tertiary hospital in Beijing that integrates medical treatment, teaching, scientific research, and prevention with 1900 beds. It has complete diagnosis and treatment methods, organizational systems, and laboratory testing conditions. The research protocol was approved by the Ethics Review Committee of Beijing Chaoyang Hospital affiliated to Capital Medical University (2023-10-17-1).

Study subjects

Male patients,who underwent HPV testing in the departments of dermatology and urology, were enrolled in the study from November 2015 to October 2023. We collected and analysed the data of male patients who were 18 years or older. Patients with unclear diagnoses and for health consultation were excluded.

We hypothesized that the expected prevalence rate of HPV was 0.1, the significance level (α) was 0.05, and the allowable error was 0.1. Excluding 10% of the healthy population visiting for the physical examination, the expected sample size was 3960.

Sample collection and DNA extraction

Genital scraped cells from the urethral epithelium, anus, or penile epidermis were collected by physicians with a nylon-flocked swab. The swab was placed in separate 3 mL tubes containing transport medium and immediately transported to a clinical laboratory affiliated with Chaoyang Hospital for HPV testing. Specimens that could not be shipped for the examination in time were stored at 4°C and analysed within 72 h. About 1 mL of sterile saline was added to the specimen test tube, shook thoroughly, sucked, and transferred to a 1.5 mL centrifuge tube. Then, the tube was centrifuged in a small high-speed centrifuge (Zhuhai Black horse Medical Instrument Co. LTD, Min1424) at 16100 g for 5 min.

The precipitate was directly added to 100 μL of nucleic acid extract and thoroughly mixed, followed by heating to 100°C for 10 min in a metal bath and centrifugation at 16100 g for 5 min, and the supernatant was used as a template for the PCR reaction.

HPV DNA genotype testing

High-risk HPV Genotyping Real-time PCR kit (Zhijiang Biotech, Shanghai, China) was used for performing HPV DNA testing. The kit used 15 specific primers and TaqMan fluorescent probes of HPV genotypes, including HPV-52/58/16/51/66/18/39/56/59/31/68/35/33/82/45. HPV testing was performed with a SLAN 96P Real-Time PCR System (Shanghai Hongshi Medical Technology, Shanghai, China) according to the manufacturer's instructions. The amplification procedure was as follows: 94°C for 2 min, followed by 40 cycles of 93°C for 10 s, and 62°C for 31 s, and single-point fluorescence was detected at 62°C. Quality control was conducted throughout the experiments, including DNA extracting and amplification by positive and negative control. The data of HPV detection results were collected for this study retrospectively.

Statistical analysis

All data were cleaned and analysed using R version 4.2.3. Age was described using the median and interquartile range (IQR). The term of age was divided into four groups as follows: < 25 years, 25–34 years, 34–44 years, and ≥ 45 years. The detection rate of HPV was calculated as the number of patients with positive results divided by the number of patients with HPV test, and a 95% confidence interval (CI) was calculated. The Chi-square test or Fisher exact test was used to explore the associations among different age groups or different genotypes. A multivariable Logistic regression model was used to explore which HPV genotypes were more likely to infect patients with different ages and clinical manifestations. All statistical tests were bilateral and $P < 0.05$ was used to determine statistical significance.

Results

The detection rate of HPV

A total of 5114 male patients with HPV detection were enrolled in the hospital in Beijing from November 2015 to October 2023. More than 80% of patients were from the urology department. The symptoms of patients were divided into warts (3.2%), prostatitis (46.3%), balanitis (25.0%), rash (6.0%), urethritis (3.7%), other urinary inflammation (7.9%), and other diagnose (7.9%). Compared with patients infected with HPV, patients without HPV infection had a lower proportion of balanitis and a higher proportion of prostatitis (Table 1).

The overall detection rate of HPV was 25.19% (1288/5114, 95% CI 24.00%−26.38%) (Figure 1(A)), and the single infection and co-infections (≥ 2 HPV genotypes) was 16.99% (869/5114, 95% CI 15.97% −18.05%) and 8.19% (419/5114, 95% CI 7.46% −8.98%), respectively. The median age among patients with negative HPV test results was 32 (IQR 25−39) years, while 33 (IQR 24−42) years among patients with a single infection of HPV and 33 (IQR 22−44) years among patients with co-infection of HPV (Table 1). The highest detection rate of HPV among four age groups was 37.08% (155/418, 95% CI 32.45%−41.71%) for ≥ 45 years, followed by 31.60% (85/269, 95% CI 26.04%−37.15%) for < 25 years, 27.55% (397/1441, 95% CI 25.24%−29.86%) for 34–44 years, and 21.80% (651/2986, 95% CI 20.32% −23.28%) for 25−34 years, respectively ($P < 0.001$). The patients from the dermatology department had a higher detection rate of HPV than those from the urology department (32.02% *vs.* 24.26%, $P < 0.001$) (Figure 1(A)). The detection rate of HPV remained stable from 2015 to 2018, rose in 2019 and remained stable thereafter. The largest proportion of the number of patients with HPV test accounted for 23.13% in 2016 with an HPV detection rate of 14.54% (172/1183, 95% CI 12.53%−16.55%), and the least proportion of the number of patients with HPV tests accounted for 4.24% in 2020 with HPV detection rate of 33.64% (73/217, 95% CI 27.35%−39.93%). The highest detection rate of HPV was 36.41% (213/585, 95% CI 32.51%−40.31%) in 2022 (Figure 1(B)). The proportion of symptoms varied from year to year. The proportion of prostatitis accounted for 58.50% in 2018, and 16.78% in 2019, and then maintained a relatively stable level (Figure 1(C)).

Distribution of HPV genotypes

Among 15 high-risk HPV genotypes tested, the top five HPV genotypes were HPV-52 (5.63%), HPV-58 (4.77%), HPV-16 (4.46%), HPV-51 (4.26%), and HPV-66 (2.85%) (Figure 2(A)). Further analysis

Table 1. Demographic characteristics of male patients with HPV detection in a hospital in Beijing from 2015 to 2023.

Variables	Total ($n = 5114$)	Negative ($n = 3826$)	Positive ($n = 1288$) Single infection ($n = 869$)	Co-infection ($n = 419$)	P^a value	P^b value
Age, years, median (IQR)	33 (25.0, 41.0)	32 (25.0, 39.0)	33 (24.0, 42.0)	33 (22.0, 44.0)	<0.001	<0.001
Clinical department, *n* (%)					1	<0.001
Dermatology	609 (11.9)	414 (10.8)	132 (15.2)	63 (15.0)		
Urology	4505 (88.1)	3412 (89.2)	737 (84.8)	356 (85.0)		
Year, *n* (%)					0.034	<0.001
2015	244 (4.8)	204 (5.3)	28 (3.2)	12 (2.9)		
2016	1183 (23.1)	1011 (26.4)	125 (14.4)	47 (11.2)		
2017	856 (16.7)	671 (17.5)	129 (14.8)	56 (13.4)		
2018	718 (14.0)	575 (15.0)	109 (12.5)	34 (8.1)		
2019	298 (5.8)	191 (5.0)	66 (7.6)	41 (9.8)		
2020	217 (4.2)	144 (3.8)	49 (5.6)	24 (5.7)		
2021	472 (9.2)	309 (8.1)	112 (12.9)	51 (12.2)		
2022	585 (11.4)	372 (9.7)	126 (14.5)	87 (20.8)		
2023	541 (10.6)	349 (9.1)	125 (14.4)	67 (16.0)		
Diagnose, *n* (%)					0.141	<0.001
Warts	163 (3.2)	105 (2.7)	41 (4.7)	17 (4.1)		
Prostatitis	2367 (46.3)	2068 (54.1)	220 (25.3)	79 (18.9)		
Balanitis	1278 (25.0)	757 (19.8)	349 (40.2)	172 (41.1)		
Rash	309 (6.0)	208 (5.4)	67 (7.7)	34 (8.1)		
Urethritis	188 (3.7)	128 (3.3)	37 (4.3)	23 (5.5)		
Other Urinary inflammation	405 (7.9)	274 (7.2)	83 (9.6)	48 (11.5)		
Other diagnose	404 (7.9)	286 (7.5)	72 (8.3)	46 (11.0)		

Note: [a]Single infection compared with multiple infections; [b]Positive compared with negative.

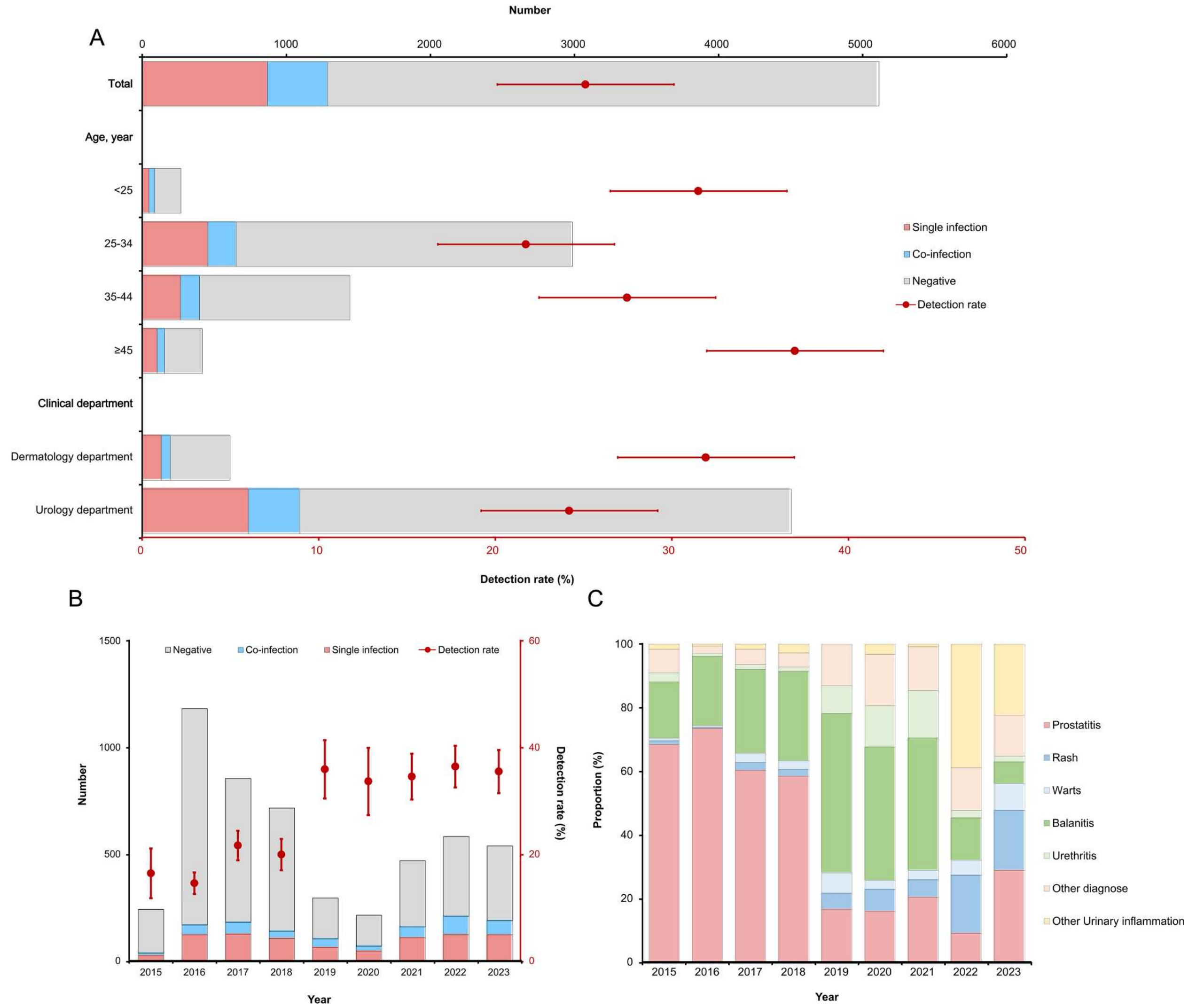

Figure 1. The number and detection rate of HPV infections. (A) The number of HPV tests and HPV detection rate of variables. (B) The number of HPV tests and detection rate of HPV in different years in China. (C) the proportion of data for each diagnosis in different years among all patients.

indicated that 5.28% (270/5114) of patients had dual infections, 1.68% (86/5114) had triple infections, and 0.78% (40/5114) had quadruple infections, and 0.45% (23/5114) had more than five genotypes' infections (Supplemental Table 1). The most common combination for co-infections of HPV observed in this study was HPV-52 and HPV-58 (Supplemental Table 2). There were significant differences in the detection rate of HPV genotypes (HPV-66, HPV-18, HPV-31, and HPV-68) among the classified age groups (all $P < 0.05$). Compared with the group aged <25 years, male patients aged ≥45 years were more likely to be infected with HPV-68 (OR = 1.019, 95% CI 1.001–1.036) and less likely to be infected with HPV-18 (OR = 0.973, 95% CI 0.949–0.997). The risk of HPV-66 infection and HPV-31 infection were both lower in the group aged 25–34 years than in the group aged <25 years (HPV-66: OR = 0.965, 95% CI 0.941–0.990; HPV-31: OR = 0.978, 95% CI 0.961–0.994). The risk of HPV-31 infection in the 35–44-old-year group was lower than that in the group aged <25 years (OR = 0.980, 95% CI 0.963–0.997) (Figure 2(B) and Supplemental Table 3). The HPV vaccines licensed currently in China market include 2-valent (HPV-16/18), 4-valent (HPV-6/11/16/18), and 9-valent (HPV-6/11/16/18/31/33/45/52/58). The estimated vaccine coverage of 2-valent and 4-valent HPV vaccine against high-risk HPV genotypes was 27.5%, with a gap of 72.5% alone. The estimated coverage of the 9-valent HPV vaccine against high-risk HPV genotypes was 81.2%, with a gap of 18.8% (Figure 2(C)).

Clinical manifestations and diagnoses

The detection rate of HPV was 40.77% (521/1278), 35.58% (58/163), 32.69% (101/309), 31.91% (60/188), 12.63% (299/2367), 32.35% (131/405), and 29.21% (118/404) among male patients with balanitis, warts, rash, urethritis, prostatitis, other urinary inflammation and other diagnose, respectively ($P < 0.001$) (Figure 3(A)). The risk of HPV genotype infection

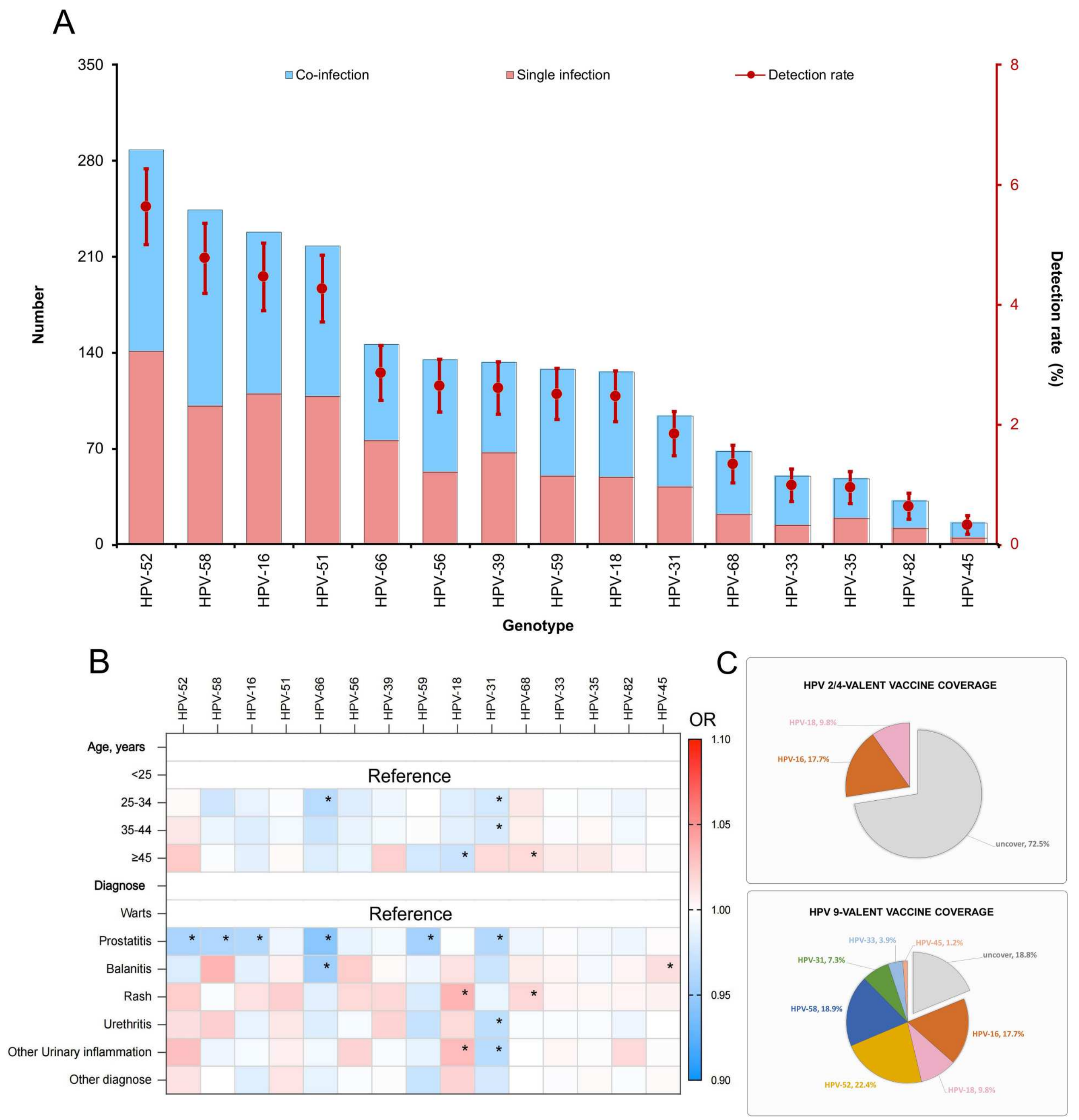

Figure 2. The number, detection rate, and multivariate analysis results of single and co-infections of each HPV genotype. (A) The number of positive cases and detection rate of HPV genotypes, ranging from the highest to the lowest by overall detection rate. (B) Heat map of the results of multivariable analyses of HPV infection by age groups and diagnostic groups. There are significant differences ($P < 0.05$) marked with * in the graph. (C) The coverage rate against high-risk HPV genotypes of the bivalent, 4-valent, and 9-valent HPV vaccine currently used in China.

was also different by clinical diagnosis. Compared with patients with warts, male patients diagnosed as prostatitis had a lower risk of HPV-52 (OR = 0.958, 95% CI 0.924–0.994), HPV-58 (OR = 0.961, 95% CI 0.928–0.993), HPV-16 (OR = 0.963, 95% CI 0.932–0.995), HPV-66 (OR = 0.944, 95% CI 0.915–0.975), HPV-59 (OR = 0.955, 95% CI 0.932–0.979), and HPV-31 (OR = 0.962, 95% CI 0.942–0.983) infection. The patients with rash and other urinary inflammation had a higher risk of HPV-18 infection and the patients with urethritis and other urinary inflammation had a lower risk of HPV-31 infection compared to those with warts (Figure 2(B) and Supplemental Table 3). The top three genotypes were HPV-51, HPV-52, and HPV-58 among patients with warts, HPV-16, HPV-52, and HPV-58 with prostatitis, HPV-52, HPV-16 and HPV-58 with balanitis, HPV-58, HPV-52 and HPV-51 with rash, and HPV-58, HPV-52, and HPV-16 with urethritis (Figure 3(B)).

HPV successive infection

Patients who had multiple visits to urology and dermatology departments for HPV testing were also analysed. After the first positive HPV test, the proportion

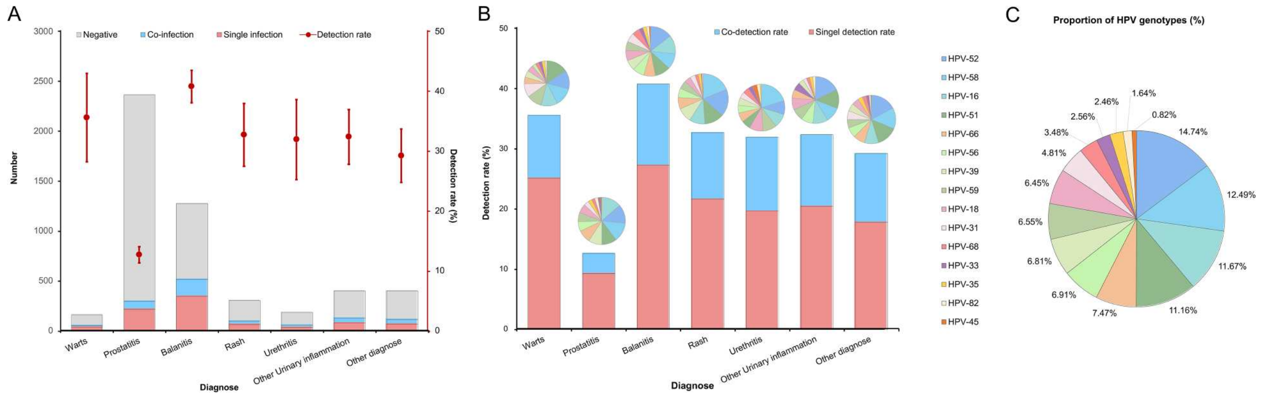

Figure 3. HPV infection in different diagnostic groups. (A) The number of HPV tests and the detection rate of HPV in each diagnostic group. (B) The proportion of HPV genotypes in total and different diagnosis groups. (C) The proportion of each HPV subtype in all positive cases.

of male patients who turned negative was 22.47% within 3 months, 26.40% within 3–6 months, 24.72% within 6–12 months, 17.98% within 12–24 months and 8.43% more than 24 months (Supplemental Figure 1A). The most common switching model of HPV genotype was from HPV-16 to HPV-52, HPV-58, and HPV-56, and from HPV-58 to HPV-66 (Supplemental Figure 1B). The HPV genotypes with the longest and shortest period from positive to negative were HPV-45 and HPV-59, respectively (Supplemental Figure 1C).

Discussion

In this study, we described the prevalence of HPV infection among male patients from urology and dermatology departments in Beijing with a large sample size and explored the distribution of 15 high-risk HPV genotypes in various groups. The high detection rate of HPV indicated that HPV still carried a significant disease burden in males.

In our study, the overall HPV detection rate was 25.19%. The prevalence of genital HPV infection among men who wished to undergo tests for HPV in the general population in Yunnan province was 23.85%, which was similar to our results [13]. A survey in Liuzhou, China showed that the overall HPV detection rate among the general male population was 10.50%, which was lower than our results [11]. Moreover, the detection rate of HPV in our result was lower than that among the high-risk population, such as 77.1% among men who had sex with men in Lima, Peru [18] and 65.5% among men who conducted in a sexually transmitted disease clinic in Shanghai [14]. These results suggested that the prevalence and genotypes of HPV infection varied by population and geographic region [19,20].

The detection rate of HPV remained at a relatively stable level before 2019. While it increased suddenly due to the change in criteria for male patients for HPV testing. Under the requirements of medical insurance, the standard of HPV testing was changed in 2019 and only patients with obvious symptoms were tested for HPV, which led to a decrease in the number of samples submitted for testing and an increase in the positive rate of HPV. Since then, the detection rate of HPV has continued to maintain a certain level. In our study, patients from urology departments accounted for 88.10% as the symptoms caused by HPV were mainly genital warts and patients were more inclined to seek treatment in the urology department [2,21].

The top five HPV genotypes were HPV-52, HPV-58, HPV-16, HPV-51, and HPV-66, which was consistent with the data generated by some Chinese population-specific investigations [4,10,11]. A study conducted in Guangdong Province, China showed that the top five prevalence of high-risk HPV genotypes among males were HPV-16, HPV-18, HPV-31, HPV-33, and HPV-35 [10]. Another study conducted in southern China showed that the most common HPV genotypes among males were HPV-58, HPV-52, and HPV-16 [11]. The dominant HPV genotypes observed in the cervical region of Chinese women were HPV-16, HPV-52, HPV-58, HPV-53, and HPV-18[8,22]. HPV-52, HPV-16, and HPV-58 are very common genotypes in both men and women. HPV-16 and HPV-18 are the most common genotypes worldwide and account for approximately 70.9% of cervical cancers [23]. However, HPV-52 and HPV-58 were more prevalent in the Asian population, in both individuals with HPV infection and cervical cancer [24–26]. Taking the current HPV vaccines licensed in China as an example, the 2-valent and 4-valent vaccines can cover 27.5% of male high-risk HPV infections with a gap of 72.5%, and the 9-valent vaccines can cover 81.2% of male high-risk HPV infections with a gap of 18.8%. Therefore, a 9-valent HPV vaccine should be recommended for men in the current situation to obtain a higher protection effect. While the positive rate was 4.26% for HPV-51, 2.85% for HPV-66, and 2.64% for HPV-56, higher than the

2.46% for HPV-18 in our study among high-risk HPV genotypes not covered by the 9-valent HPV vaccine, it is still necessary to develop a more broad-spectrum HPV vaccine targeted to China or Asian or even different area in the future, to fill the protection gap against high-risk HPV genotypes.

The detection rate of HPV showed an age-dependent trend [22,27] with two peaks in patients aged <25 years and ≥45 years. Peng *et al.* also observed the detection rate of HPV among male patients peaked at the age of ≤20 years (60%) and 55–59 years (50.70%) [10]. A study reported that the HPV detection rate among females peaked in the group of 20–24 years and 45–59 years in China [8], which indicates that age trends in HPV infection are similar in men and women. The 13–15 reason was that people under 25 years had more exposure opportunities [17] and immature immunity to HPV [28], and people over 45 years have weakened immunity [13].

HPV can cause many types of skin diseases and disorders, ranging from benign warts to various cancers [2,29]. In our study, the highest detection rate of HPV was observed in the patients with balanitis. Takahashi *et al.* found an 18.5% prevalence of HPV infection in men with urethritis, which was significantly higher than 7.5% in the healthy population and suggested that the reason for the difference was that more high-risk sexual behaviours increased the risk of genital system inflammation and HPV infection [30]. Balanitis and HPV infection are risk factors for squamous cell carcinoma of the penis [31]. A study in Suzhou, China showed verruca, urethritis, and balanitis patients has more frequent concurrence of high-risk HPV infection in men. This prodromal disease is now thought to be associated with sexually transmitted HPV infection [32]. By investigating microorganisms in prostate secretions in patients with chronic prostatitis and normal young men, Xiao *et al.* found that HPV infection might be related to the degree of inflammation within the prostate by key measures such as lecithin and white blood cells, and the HPV detection rate of patient with prostate was 12.6% in this study which was similar to 12.63% in ours [33]. These studies suggest that the mechanism of the co-occurrence of HPV infection and inflammation of the reproductive system still needs to be studied to clarify the necessity of strengthening general screening for HPV. At present, there is no very effective method to eradicate HPV. Physical methods are mainly used to remove warts for patients with condyloma acuminatum caused by HPV [34]. For women, HPV vaccination is an effective and safe measure to prevent HPV infection [35], but for men, HPV vaccine is not available yet in China.

Our study showed that 26.41% of patients took more than one year for HPV clearance while 36.0% in a study among gay, bisexual, and other men who have sex with men [36]. The longest clearance time of HPV was 13.4 months for HPV-45, followed by 8.4 months for HPV-16, and 8.1 months for HPV-31. The patient's immune function, HPV infection site, and the treatment for HPV infection have effects on the time to viral conversion to negative [37–41]. In most infected people, HPV is cleared by the immune system within a few years of onset. However, viral infections may continue to lurk in some populations. These patients with persistent HPV infection have an increased chance of developing epithelial cell abnormalities and subsequently developing cancer at the site of infection [37,38]. Persistent HPV infection is associated with cervical, anogenital, and head and neck cancers [39,40]. A systematic review showed that conectomy and annulectomy were superior to cryotherapy in their ability to clear HPV infection within 12 months of treatment [41]. A cohort study of oral HPV infection in men showed that the longest median clearance time was 7.6 months for HPV-33, followed by 6.4 months for HPV-16 and HPV-45 [42]. Considering that the clearance time was counted from the date of the first HPV-positive test in our study, this could be the cause of the difference. To date, the mechanism of co-infection and mutual conversion between HPV genotypes is still being explored. Previous studies showed that persistent HPV infection and the risk of recurrence may be related to genetic variants [43]. The expression of E6 and E2 proteins may be the key factors for the sustained infection of HPV in epithelial cells [44]. However, people with persistent HPV infection should pay attention to monitoring their HPV infection to detect possible lesions as early as possible.

There were some limitations in this study. First, it was a single-centre study including data only from one hospital. Second, we only tested 15 high-risk HPV genotypes and have not tested low-risk HPV genotypes, hence the real detection rate of HPV may be underestimated. Third, due to the limited visits, it was not possible to know how long to be infected with HPV before the first positive HPV test result, which biased the period from positive to negative for HPV. Furthermore, we did not obtain data such as immune function, specific sampling sites for HPV tests, and the treatment situation of patients, so we could not conduct a more in-depth analysis of factors of HPV persistent infection.

Conclusions

The detection rate of HPV among male patients from urology and dermatology departments in Beijing was high. HPV-52 and HPV-58 were the top two HPV genotypes, which should be paid more attention to developing more protective HPV vaccines to improve the effect of HPV prevention in the future.

Ethics approval

This study was approved by the Ethics Review Committee of Beijing Chaoyang Hospital affiliated to Capital Medical University (2023-10-17-1).

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Author contributors

QBL, FC and LG provided the conception of the study. SW, MW and PW collected the epidemiological data, samples and conducted laboratory tests. SW, QYM, JD cleaned, analysed, and interpreted the data, and QYM drafted the manuscript. TTW, WXZ and YGZ participated in the design of the study and performed the statistical analysis. LG, QBL and FQC provided critical revision of the article for important intellectual content. All authors read and approved the final version.

Disclosure statement

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Data availability statement

The study design, protocol, and statistical analysis are provided in the main manuscript and the supplementary data files. Access to the data generated and analysed in this study will be provided upon reasonable request to the corresponding author.

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