Original Article

Cervical Infection of Oncogenic Human Papillomavirus (HPV) Types in Beijing, China*

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Abstract

Objective This study was designed to determine the prevalence of oncogenic human papillomavirus (HPV) in cervical infections in Beijing, China, and to investigate the odds ratio (*OR*) of HPV single and multiple infections in abnormal cytology.

Methods A total of 19,018 specimens from outpatients in the department of obstetric and gynecology were collected. They were detected using high-risk HPV genotyping real-time polymerase chain reaction (PCR) kit and analyzed by ThinPrep cytology test for cervical pathological diagnosis. HPV prevalence, age-specific prevalence, and *OR* of each type of HPV in abnormal cytology were analyzed.

Results Overall, 19.1% (3,623/19,018) of the individuals were positive for HPV infection, 14.9% (2,833/19,018) were positive for a single HPV type, and 4.2% (790/19,018) were positive for multiple types. Among the 3,623 HPV-positive individuals, the most predominant HPV types were HPV52 (4.4%, 834/19,018), HPV16 (3.7%, 710/19,018), and HPV58 (3.4%, 644/19,018). The *OR* of multiple infections and single infection differed significantly among disease severities. The *OR* of dual infection was higher than that of each of the two single infection types, respectively.

Conclusion HPV prevalence in the outpatients was 19.1%, and the most predominant HPV types in the study were HPV52, HPV16, and HPV58. Women with multiple infectionswere more likely to have abnormal cytology.

Key words: Cervical cancer; HPV; TCT; LSIL; HSIL; Odds ratios

Biomed Environ Sci, 2016; 29(10): 734-741 *doi: 10.3967/bes2016.098* *ISSN: 0895-3988*

www.besjournal.com (full text) *CN: 11-2816/Q*

INTRODUCTION

Cervical cancer (CC) is the second most common malignant disease and a leading cause of cancer mortality among women worldwide[1]. The causal link between human papillomavirus (HPV) infection and CC is now established beyond doubt. HPVs are small DNA viruses having a circular double-stranded DNA genome of approximately 8 kb, and they are classified on the basis of their genome DNA sequence. An HPV type has <90% similarity with other types at the

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[*] This work was supported by National Science and Technology Major Project funded by the Chinese government [2013ZX10004-101].

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nucleotide level[2-3].

Based on their association with CC and precursor lesions, HPVs can be grouped into high-risk, possible high-risk, and low-risk HPV types[4]. The high-risk HPV (HR-HPV) infection accounts for 43%-53% of patients with cervical intraepithelial neoplasia (CIN) in the western population[5-6]. HPV screening is strongly advised because of the important role of HPV in the development of CC and other associated diseases and its greater sensitivity and cost-effectiveness in detecting CC. Screening for HR-HPV may reduce the risk for CC. HPV16 and HPV18 are two predominant prevalent types associated with CC in western countries[7]. HPV prevalence data of some regions of China suggest that the distribution of HPV types is different in China[8-11].

Cervical coinfection with more than one HPV genotype is common. Nonetheless, it is unclear whether any two HPV types are more or less likely to be involved in a coinfection. The role played by coinfections with multiple HPV types in cervical neoplasia remains a difficult area of investigation. Some studies have shown that the risk for cervical precancerous lesions or invasive cancer in women infected with multiple HPV types is no greater than that in those with single-type infections, while some studies have shown that infection with multiple HPV types appears to act synergistically in cervical carcinogenesis[12-15]. With the increasing administration of HPV prophylactic vaccines, the mechanism behind multiple-type infections warrants further investigation, in light of the concern for HPV type replacement.

The purpose of this study was to investigate the prevalence of HR-HPVs and the frequency of single and multiple infections and to investigate the different risk of cervical lesion severity between HPV single and multiple infections. The interaction between different phylogenetic species in dual infection was also analyzed to assess the presence of any biological interactions between species that contribute to multiple-type infections.

MATERIALS AND METHODS

Subjects

A total of 19,018 patients were studied from January 2013 to July 2014 in the department of obstetric and gynecology at the Chinese PLA General Hospital in Beijing. All the 19,018 patients underwent high-risk HPV DNA quantitative measurement and biopsy. Among them, 17,790 individuals were diagnosed as normal, 959 patients were diagnosed with atypical squamous cells of undetermined significance (ASCUS), 93 patients were diagnosed with low-grade squamous intraepithelial lesion (LSIL), and 176 patients were diagnosed with high-grade squamous intraepithelial lesion (HSIL).

Pathological Examination

Cervical cytology was carried out by ThinPrep cytology test (TCT). Cytological diagnosis was made according to the Bethesda system classification. Histological diagnosis of the cervix was made according to the criteria proposed by the 7th edition of 'Obstetrics and Gynecology'. The biopsy of pathological sections was reviewed by senior physicians.

HPV Detection and Genotyping

DNA extraction and HPV genotyping were carried out using high-risk HPV genotyping real-time PCR kit (Shanghai ZJ Bio-Tech Co., Ltd) to detect the following HPV types: HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68. The lowest detection limit of the kit was 1×10^4 copies/mL. Amplification techniques performed on SLAN®-96P (Shanghai Hongshi Medical Technology Co., Ltd) were used for the quantitative estimation of HPV DNA copies.

Statistical Analysis

All statistical analyses were performed using SPSS statistical software version 19.0. The data were stratified by age (≤20 years, 21-25 years, 26-30 years, 31-35 years, 36-40 years, 41-45 years, 46-50 years, 51-55 years, 56-60 years, and ≥61 years). Chi-squared analyses were used for bivariate comparisons between age groups. $P<0.05$ was considered as statistically significant. Logistic regression was used to estimate the odds ratio (*OR*) with 95% confidence intervals to examine the association between HPV infection and CIN risk.

RESULTS

Prevalence of the Oncogenic Genotypes in the Cervical Samples

Real-time PCR quantification assays were used to investigate the frequency of type-specific HPV infection. Among the 19,018 patients, positive HPV test were obtained in 3,623 (19.1%, 3,623/19,018) patients, of whom 2,833 (14.9%, 2,833/19,018) were positive for a single HPV type and 790 (4.2%,