Original Article

Prevalence of HPV Infection And Cervical Intraepithelial Neoplasia And Attitudes towards HPV Vaccination among Chinese Women Aged 18-25 in Jiangsu Province

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ABSTRACT

Objective: Few data are available on the epidemiology of HPV and cervical cancer among Chinese women younger than 25 years old. This study aimed to estimate the HPV infection rate and the prevalence of cervical intraepithelial neoplasia (CIN) in women aged 18-25, as well as their knowledge of and attitudes towards HPV vaccination.

Methods: A population-based cervical cancer screening study was conducted on women aged 18-25 in Jiangsu province in 2008. Participants provided socio-demographic, reproductive and behavioral information and completed a survey about their knowledge of and attitudes towards HPV vaccination. Women then underwent a gynecologic exam to provide two cervical exfoliated cell samples for high risk HPV DNA testing and liquid-based cytology (LBC) as well as visual inspection with acetic acid (VIA). Women testing positive for any test were referred to colposcopy and biopsy. The gold standard for diagnosis of cervical lesions was directed or random biopsies.

Results: Within the sample of 316 women, 3.4% of them were diagnosed with CIN grade 2 or worse lesions and 17.1% were found to be positive for HPV DNA. Among these young women, extra-marital sexual behavior of them (OR=2.0, 95%CI: 1.1-3.8) or their husbands (OR=2.6, 95%: 1.4-4.7) were associated with an increased risk of HPV positivity. Although overall HPV awareness was low, after a brief educational intervention, 98.4% reported they would electively receive HPV vaccination and would also recommend that their daughters be vaccinated. However, most urban and rural women reported their ideal maximum out-of-pocket contribution for HPV vaccination to be less than 500 RMB and 50-100 RMB, respectively.

Conclusion: Our study indicates cervical disease burden is relatively high among sampled Chinese women aged 18-25. Appropriate educational interventions for female adolescents and strategies to subsidize vaccine costs are definitely needed to ensure the effectiveness of vaccination campaigns in China.

Key words: Cervical cancer; Cervical intraepithelial neoplasia; Human papillomavirus; Knowledge; Attitude

INTRODUCTION

Cervical cancer is the second most common cancer among women worldwide, with an estimated 88% of the annual incidence occurring in developing countries[1]. The People's Republic of China accounts for 14% of the world's annual incidence of cervical cancer (75,500 new cases) and 12% of the world's annual mortality from cervical cancer (34,000 deaths)[1]. The etiology of cervical cancer, and precancerous cervical intraepithelial neoplasia (CIN) has been clearly established as high-risk human papillomavirus (HPV)[2, 3]. Multiple studies have demonstrated that the prevalence of CIN and HPV infection varies by age[4-6]. Though several population-based screening studies reported the prevalence of HPV infection and CIN in China[7-13], most studies focused on women older than 30 or 35. Very few data exist describing HPV and CIN prevalence among Chinese women younger than 25 years old.

The well-established etiology of cervical cancer has allowed for the development of HPV vaccines as primary

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cervical cancer prevention methods. Currently, two prophylactic HPV vaccines are commercially available, Gardasil (Merck & Co., USA) and Cervarix (GlaxoSmith-Kline, Belgium). Both vaccines target HPV-16 and -18, which cause 70.1% of invasive cervical cancers worldwide[14-16]. The Gardasil vaccine additionally targets HPV-6 and -11, responsible for about 83% of genital warts[17]. These HPV vaccines are heralded to be promising methods to decrease HPV infection and cervical cancer incidence and have been widely utilized in many developed countries. However, in order to achieve significant reduction in worldwide cervical cancer incidence, the HPV vaccine must be introduced in low-resource countries as well. Both vaccine companies are currently conducting clinical trials in China and preparing to apply for approval from State Food and Drug Administration. To assess the potential impact HPV vaccines may have in China, it is imperative to determine the burden of HPV infection and cervical disease in young Chinese women.

To address this gap in knowledge, we conducted a population-based cervical cancer screening study examining 316 women aged 18-25 in Jiangsu Province from June to August, 2008. Our study aimed to estimate the CIN prevalence and HPV infection rate by cytology and histology in this population. In addition, we conducted quantitative surveys to determine participants' knowledge of and attitudes towards HPV infection, cervical cancer, and HPV vaccination in order to determine major obstacles facing future vaccination campaigns in China.

MATERIALS AND METHODS

Study Subjects

This population-based cross-sectional study targeted the female population aged 18-25 in Jiangsu Province, China, using a cluster sampling design with the commune as the unit of cluster. Research was conducted at three investigational sites: one rural site (Binhai County), one suburban site (Jintan County), and one urban site (Xuzhou City). Eligible women were mentally and physically competent, sexually active, not pregnant, with an intact uterus and had no history of CIN, cervical cancer, or pelvic radiation. Menstruating women were excluded until menstruation finished. All women provided written informed consent. This study was approved by the Institutional Review Board of the Cancer Foundation of China.

Study Procedure

Local health workers recruited women via door-to-door solicitation. All eligible women were invited to participate in the study at the local clinic. At the initial research visit, women were informed about the study's risks and benefits, research procedures, and confidentiality assurance, and those who agreed to participate then provided written informed consent. Prior to the clinical examination, trained health-care workers reassessed participants to ensure eligibility before asking them in a private setting about socio-demographic, reproductive and behavioral information. Participants then completed a survey about HPV infection and attitudes to HPV vaccination.

After the interviewer-administered questionnaire, a gynecological examination was conducted to collect two vials of exfoliated cervical cell samples for liquid-based cytology (LBC) (ThinPrep®, Hologic, Bedford, MA, USA) and high-risk HPV DNA testing before conducting visual inspection with acetic acid (VIA). Women who were VIA positive or suspicious for cancer (SFC) received colposcopy (Goldway, Shenzhen China) with directed biopsies. Women were called back for colposcopy two weeks after the initial visit if they had negative VIA but positive HPV DNA test or cytology results of atypical squamous cells-cannot exclude high-grade squamous intraepithelial lesion (ASC-H) or low-grade squamous intraepithelial lesion and worse (LSIL+). Directed biopsies were taken for women with positive HPV and negative or atypical squamous cells of undetermined significance (ASC-US) on cytology if colposcopy findings were abnormal. Directed and random biopsies were both done for the women with ASC-H or LSIL+ on cytology (For abnormal quadrants, the most abnormal areas received directed biopsy. For normal quadrants, random biopsies of the squamo-columnar junction (SCJ) were taken at two, four, eight and ten o'clock)[7]. If the SCJ could not be visualized with colposcopy, endocervical curettage (ECC) was performed. Patients with CIN grade 2 or worse (CIN2+) lesions were treated according to local medical standards.

Oncogenic HPV DNA Testing

Carcinogenic HPV DNA testing was performed using the high-risk probe set of Hybrid Capture 2 (HC2, Qiagen Inc., Gaithersburg, MD, USA), which detects 13 carcinogenic HPV types (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68). The HC2 sampling device was placed in preservative solution, stored at room temperature, and transported to the HPV lab at the Cancer Institute, Chinese Academy of Medical Sciences (CICAMS), where certified technicians performed the HC2 test. Results were expressed in relative light units (RLU) and compared with the mean RLU from a minimum positive control set at 1.0 pg/mL. Samples ≥1.0 were positive, and <1.0 were negative.

Cytology Diagnosis

The cytology sampling device was placed in PreservCyt liquid-based cytology preservative medium, stored at room temperature, and transported to CICAMS, where processing, staining and classification was performed according to the Bethesda system[18]. Samples were read as being within normal limits (negative), ASC-US, atypical glandular cells of uncertain significance (AGC), ASC-H, LSIL, high-grade squamous intraepithelial lesion (HSIL), squamous cell carcinoma (SCC), adenocarcinoma in situ (AIS), or adenocarcinoma (ADC). A junior cytopathologist diagnosed all slides before a senior cytopathologist reviewed them for