Original Study

Genital HPV in Children and Adolescents: Does Sexual Activity Make a Difference?

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A B S T R A C T

Study Objective: To compare the prevalence of human papillomavirus (HPV) genital infection among prepubertal children, sexually active and not sexually active adolescents, and assess potential risk factors for transmission.
Design: Prospective study.
Setting: Outpatient adolescent health clinic.
Participants: Ninety-five girls aged 2-21 years; 38 sexually active adolescents (group A), 28 not sexually active adolescents (group B), and 29 prepubertal children (group C).
Interventions: Participants' vaginal or cervical specimens were tested for HPV with the CLART HPV 2 assay (Clinical Array Technology, Genomica, Madrid, Spain) and for cytological abnormalities with liquid-based cytology.
Main Outcome Measures: Differences in prevalence of low- and high-risk HPV infections among the 3 groups.
Results: Genital HPV was detected in 37.9% (36/95) of all participants; 47.4% (18/38) of group A, 28.6% (8/28) of group B, and 34.5% (10/29)of group C ($P = .27$). Multiple HPV infection was detected in 26.3% (10/38), 10.7% (3/28), and 13.8% (4/29) of groups A, B, and C, respectively ($P = .21$). High-risk genotypes were detected in 47.4% (18/38), 28.6% (8/28), and 24.1% (7/29) of groups A, B, and C, respectively ($P = .10$). Main high-risk genotypes were HPV 16 (27%, 10/37), HPV 31 (21.6%, 8/37), HPV 35 (13.5%, 5/37), HPV 53 (13.5%, 5/37), and low-risk HPV 6 (18.9%, 7/37). Sexual activity was associated with increased risk for genital high-risk HPV infection (odds ratio = 3.41; 95% confidence interval, 1.19-9.78); specifically with HPV 33 and HPV 51. Forty percent of sexually active adolescents with normal cervical cytology were infected with high-risk HPV types. Family history of skin HPV was positively associated with genital HPV in the sexually active group (odds ratio = 2.01; 95% confidence interval, 1.17-3.46).
Conclusion: Timeline and target population for HPV vaccination might need to be reappraised, in view of significant nonsexual transmission of genital HPV so early in childhood.
Key Words: HPV, Prepubertal girls, Children, Adolescents, Sexual activity, Epidemiology, Greece

Introduction

Human papillomaviruses (HPVs) are associated with a wide variety of cutaneous and mucosal infections and with malignancies in humans. More than 100 HPV types have been identified, some of which have affinity for skin and others for mucosal sites.[1] Different HPV types can cause common warts, anogenital warts, respiratory papillomatosis, low- or high-grade squamous intraepithelial cervical lesions, and cervical, anogenital, or oropharyngeal malignancies. HPV genotypes designated as low risk are usually associated with the development of skin warts and noncarcinogenic lesions and high-risk genotypes are associated with cancers.[2]

Genital HPV infection is considered mainly a sexually transmitted disease. Its incidence increases after the first sexual intercourse and female adolescents who are sexually active have particularly high rates of infection.[3–5] Many countries have introduced HPV vaccination in the vaccination program of adolescent girls and young women, as a preventive measure against HPV-related cancers and infections.[6]

Nevertheless, the modes of HPV transmission in children and in not sexually active adolescents remain controversial.[7,8] Several potential modes of transmission for pediatric HPV infections include perinatal transmission, auto- and heteroinoculation, and possibly, indirect transmission via fomites.[9] These nonsexual modes of transmission have an important effect on vaccination strategies and clinical management of children with HPV-associated diseases.[10]

Although several studies have investigated the epidemiology and natural history of HPV infection in sexually active adolescents and adults, limited data exist for genital

The authors indicate no conflicts of interest.

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HPV infection in prepubertal children and not sexually active adolescents. The aim of this study was to compare the prevalence of HPV genital infection among prepubertal children, sexually active and not sexually active adolescents, and assess potential risk factors for transmission.

Materials and Methods

Study Population

This was a pilot prospective study, conducted at the Center for Adolescent Medicine and United Nations Educational, Scientific and Cultural Organization (UNESCO) Chair on Adolescent Health Care of the First Department of Pediatrics of the Athens University Medical School, from September 2012 to September 2014. Female children, sexually active and not sexually active adolescents who presented at the outpatient clinic of Center for Adolescent Medicine for gynecologic assessment were eligible for participation in the study. Gynecologic assessment included cervical cytology screening for the sexually active girls because there is no age restriction in Greece. Sexual activity was defined as any sexual intercourse that included vaginal penetration. Girls or adolescents with no history of sexual activity (ie, vaginal [penile, digital, or oral], anal, or oral intercourse), were considered not sexually active. Exclusion criteria included pregnancy or sexual abuse.

Participants and/or their guardians gave written informed consent to undergo clinical anogenital examination and to be included in the study. The study was in accordance with the Declaration of Helsinki and was approved by the Ethics Research Committee of the First Department of Pediatrics.

Study Procedures

For all participants a detailed social, family, and medical history was obtained, including details regarding risk factors, personal, and family history of HPV genital or skin infections (ie, presence of warts and previous abnormal Papanicolaou smear results). Girls underwent a thorough clinical examination including measurement of weight, height, and assessment of pubertal status by a designated adolescent medicine pediatrician. The anogenital area was carefully examined and vaginal smears were obtained with cotton swabs from all children and not sexually active adolescents. For sexually active adolescents vaginal swabs and cervical smears using an endocervical brush were obtained. For each participant a glass slide was prepared for gram stain and a vaginal swab was sent for culture; additional vaginal samples for a 'wet mount' were obtained from each adolescent.

HPV Genotyping

Vaginal and cervical specimens were placed and stored in ThinPrep Cytyc PreservCyt solutions according to the manufacturer's guidelines. A liquid-based cytology (ThinPrep Pap-Test; Hologic) sample was collected and a monolayer smear was prepared using a TP 2000 processor and stained according to Papanicolaou. An aliquot containing 1 mL of the liquid-based cytology sample was removed and prepared for DNA extraction following the manufacturers' instructions. Specimens were tested with the CLART HPV 2 kit (Clinical Array Technology, Genomica, Madrid, Spain), which allowed the detection of up to 35 different HPV types: 6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 43, 44, 45, 51, 52, 53, 54, 56, 58, 59, 61, 62, 66, 68, 70, 71, 72,73, 81, 82, 83, 84, 85, and 89. The diagnostic sensitivity and specificity of the CLART HPV 2 kit were 98.2% and 100%, respectively. Classification of high- and low- or intermediate-risk HPV genotypes was done according to International Agency for Research on Cancer (IARC).[11]

Statistical Analyses

For the statistical analyses χ^2 test and/or Fisher exact tests were used to examine associations between qualitative variables. Statistical significance was set at $P < .05$ for all statistical tests. Log linear regression models were used to control for confounding factors. Data were analyzed using Statistica version 8 (StatSoft Inc).

Results

Demographic and Baseline Characteristics

A total of 103 girls were initially included in the study. Eight children with symptoms of vulvovaginitis were excluded from the study because of their lack of cooperation, that did not allow additional vaginal samples for HPV to be obtained. Finally, the study population included 95 participants aged 2-21 years who were divided into 3 groups; group A (sexually active adolescents, n = 38; 40% of the total sample), group B (not sexually active adolescents, n = 28; 29.5%), and group C (prepubertal children, n = 29; 30.5%). Descriptive data of participants' characteristics are presented in Table 1.

The mean age ±SD for group A, B, and C was 16.4 ± 2.48 (range, 10-21) years, 13.4 ± 2.20 (range, 11-19) years, and 8.2 ± 2.40 (2-10) years, respectively.

Most sexually active adolescents presented for routine annual gynecologic examination, and most of the not sexually active adolescents (n = 20, 71.4%) and children (n = 27; 93.1%) presented with symptoms of vulvovaginitis (ie, discharge, pruritus, burning sensation, or erythema).

Most girls resided in urban areas; 43.2% were delivered by cesarean section, 34.7% participated in sports, 13.7% used disinfectants in the anogenital area, and 9.5% reported daily panty liner use.

Reported mean age of sexual debut was 15.3 years. Most sexually active adolescents (86.8%) had not received any HPV vaccine shot. Only 1 (2.6%) was fully vaccinated and 4 (10.5%) were partially vaccinated. A minority proportion of sexually active adolescents reported use of oral contraceptives (15.8%), systematic use of tobacco (39.5%), alcohol (13.2%), or illegal substance use (ie, narcotics, marijuana; 5.3%).

Family history of skin or genital warts was present in 10.6%, 7.1%, and 27.6% of girls in groups A, B, and C,