Human papillomavirus genotypes and their prevalence in a cohort of women in Trinidad

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ABSTRACT

Objective. *Human papillomavirus (HPV) genotypes and their relative prevalences were determined in a cohort of 310 sexually active women in Trinidad, West Indies.*

Methods. *Cervical samples were collected with Ayre's spatulas and endocervical brushes. Samples were used for the conventional Papanicolaou test and for determining HPV genotypes by amplification of a section of the viral L1 gene, followed by DNA sequencing and probe hybridization.*

Results. *HPV infections were identified in 126 of 310 (40.6%) women. Of them, 83 (65.8%) were infected with high-risk HPV, 16 (12.7%) with low-risk HPV, and 27 (21.4%) with HPV types of unknown risk. HPV 52 (12.7%) was the most frequently occurring high-risk type, followed by HPV 66 (10.3%), HPV 16 (9.5%), and HPV 18 (8.6%). High-risk types HPV 16 and HPV 66 were each found in 3 (20.0%) and HPV 18 was found in 1 (6.6%) of the 15 women with abnormal cytology.*

Conclusions. *Cervical HPV prevalence and heterogeneity of HPV genotypes are high in this Trinidad cohort. The relative importance of HPV genotypes in the development of cervical lesions needs further investigation in Trinidad in order to better understand the epidemiology of HPV infections as well as to determine the role of HPV testing in the screening, prevention, and control of cervical cancer. This pilot study provided important information on the prevalence of HPV genotypes, which will be used in future nationwide studies.*

Key words Cervix neoplasms, prevention; papillomaviridae; prevalence; Caribbean; Trinidad and Tobago.

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Human papillomavirus (HPV) has been recognized as a common sexually transmitted infection, etiologically linked to > 95% of cervical cancers worldwide (1). The premalignant lesions for cervical cancer are strongly associated with infection of the cervix by HPV of which there are more than 100 known types; 25 of them are proven or likely human carcinogens and can cause cancer of the cervix and other sites (2). Persistent infection with certain types of HPV can be regarded as a necessary condition for the development of cervical cancer worldwide (3). Some HPV types are considered low risk, meaning that they are not associated with progression of lesions to invasive cancer. Low-risk types of HPV can cause genital

warts and benign or low-grade cervical cell changes that result in mild Papanicolaou (Pap) test abnormalities (4). These abnormalities are rarely associated with cervical cancer. Other types are considered high risk as they are associated with progression of lesions to invasive cervical cancer. Common high-risk types of genital HPV include types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82 (5). Vaccines for prevention of HPV 16 and HPV 18 are now available but are indicated for persons not infected with the virus (6).

Cervical cancer is the second most common cancer in women in the twin-island Republic of Trinidad and Tobago, with high mortality rates among those affected.[5] Limited information is available on distribution of the HPV genotypes associated with the disease in this population. A study of 212 mainly Afro-Caribbean women from Tobago showed a high prevalence of cervical HPV infection, with HPV 45 rather than HPV 16 or HPV 18 being the most common high-risk genotype (7). No similar study has been conducted for Trinidad. There are distinct demographic differences between the islands in terms of ethnicities, degree of urbanization, and dependence on tourism, all of which may result in differences in the HPV prevalence and genotype circulation between the islands.

The Ministry of Health of Trinidad and Tobago has recognized cervical cancer as a major public health problem and wishes to implement a comprehensive prevention program. Information on the prevalence of high-risk HPV genotypes in the Trinidad and Tobago population can help to inform public health decisions about the use of HPV vaccines in this population. The information will be useful in the development of policies for cervical cancer prevention and control. The findings of such a study will also contribute to the growing knowledge of global HPV heterogeneity and inform vaccine development against HPV.

The primary objectives of this study were to provide a preliminary estimate of the prevalence of cervical HPV infection in a cohort of sexually active women aged 18 to 65 years in Trinidad and to determine the genotypes of cervical HPV and their distribution within the sample. In addition, efforts were made to identify whether there were risk factors associated with HPV infection within the cohort.

MATERIALS AND METHODS

Recruitment of participants and interview process

Participants were recruited from three primary health care centers in the populous northern part of the island in August and September 2007. Participation in the study was voluntary. All those presenting for participation were assessed for eligibility for inclusion. Exclusion from the study was based on age (< 18 years or > 65 years), current pregnancy, and previous diagnoses or treatment for cervical cancer. Written informed consent was obtained from participants before they were interviewed by trained personnel using a structured questionnaire to collect demographic information and information on possible risk factors for HPV infection. Ethical approval for the study was obtained from the Trinidad and Tobago Ministry of Health ethics committee. A total of 310 women were recruited.

Sample collection

Smears of exfoliated cells from the cervix were collected with an Ayre's spatula and endocervical brush (Andwin Scientific no touch one-slide Pap smear kit). The slides were immediately sprayed with fixative for later testing using the standard Pap test (8, 9). The Ayre's spatula and endocervical brush were then rinsed with vigorous stirring in 20 mL of Dulbecco's phosphate-buffered saline with 1% penicillin/streptomycin/Fungizone (DPBS/1% PSF) in sterile 50-mL screw-capped Falcon tubes to provide cells for HPV genotyping. Samples were stored in Styrofoam cooler boxes with frozen gel packs and transported to the laboratory within 8 hours of collection.

Sample processing for HPV genotyping

The cell suspensions were centrifuged at 1 520 × *g* (Beckman TJ-6 benchtop centrifuge) for 7 minutes, the supernatant was discarded, and the pellets were resuspended in 1 mL of DPBS/1% PSF, divided into two 500-µL aliquots, and stored at –70°C until ready for use in DNA extraction.

Each 500-µL aliquot of the cervical cell suspension was diluted to a volume of 1 mL with phosphate-buffered saline, pH 7.4. One-half of this volume was used for automated DNA extraction on the EasyMag platform, according to the procedure recommended by the manufacturer (Biomerieux). Extracted DNA was eluted in 60 µL of EasyMag extraction buffer 3 (Biomerieux).

HPV amplification

The presence of HPV DNA in cervical cell suspensions was determined by a nested polymerase chain reaction (PCR), with a first round amplification of the L1 region of the HPV genome with the MY09/MY11 consensus primers (10), followed by a second round amplification of the first round products with GP5+/GP6+ primers (11). The GP6+ primer was modified at the 5' end by conjugation with biotin and the introduction of phosphothioate bonds between the last five nucleotides for Luminex detection, as described below. The first round PCR was performed in a 50-µL reaction volume containing 5 µL of extracted DNA; 200 µM Tris hydrochloride, pH 8.4; 500 µM potassium chloride; 4 µM magnesium chloride; 200 µM each deoxyadenosine triphosphate, deoxycytidine triphosphate, deoxyguanosine triphosphate, and deoxythymidine triphosphate; 0.5 µM each MY09 and MY11 primers; and 2.5 units of Taq polymerase (Invitrogen). An initial denaturation step was carried out at 94°C for 5 minutes, followed by 30 cycles of 94°C for 30 seconds, 55°C for 30 seconds, and 72°C for 1 minute. A final extension step was carried out at 72°C for 7 minutes.

The second round PCR was performed in a 100-µL reaction volume using 2 µL of the first round reaction mixture and the same reagent concentrations as for the first round reaction. The cycling conditions were 94°C for 5 minutes, followed by 30 cycles of 94°C for 30 seconds, 40°C for 20 seconds, and 72°C for 30 seconds. A final extension step was carried out at 72°C for 7 minutes.

Amplification of the β globin gene was used to assess the quality of the DNA extracts, according to Goleski et al. 2008.[6] Products were visualized through gel

[5] Ministry of Health of Trinidad and Tobago, National Cancer Registry of Trinidad and Tobago. Cancer in Trinidad and Tobago 2000–2002. 2004.

[6] Goleski VA, Dawood M, Ratnam S, Severini A. Luminex®-based assay for multiplex genotyping of 45 mucosal human papillomavirus types. Eurogin 2008 Conference, Nice, France, 12–15 November.

electrophoresis on a 2% agarose gel stained with ethidium bromide for both the HPV and the β globin PCRs.

HPV genotyping

HPV genotypes were determined by DNA sequencing and probe hybridization at the National Microbiology Laboratories, Public Health Agency of Canada (Manitoba). The results of both genotyping methods were merged to give the final list of HPV genotypes occurring in the study population.

Nested HPV amplicons were purified by using Microcon YM-30 purification columns (Ambion) according to the manufacturer's instructions. Both strands were sequenced by automated DNA sequencing at the National Microbiology Laboratories' DNA core facility. The DNA sequences were aligned against the GenBank database using the BLAST algorithm (National Center for Biotechnology Information, Bethesda, Maryland, United States of America). HPV genotype assignment was made if > 90% identity was found on a minimum sequence length of 60 nucleotides.

Probe hybridization using xMAP® technology (Luminex Corporation) to identify 45 mucosal HPV types (6, 11, 13, 16, 18, 26, 30, 31, 32, 33, 35, 39, 40, 42, 43, 44, 45, 51, 52, 53, 54, 56, 58, 59, 61, 62, 66, 67, 68, 69, 70, 71, 72, 73, 74, 81, 82, 83, 84, 85, 86, 87, 89, 90, 91) was performed according to an in-house microsphere-based assay.[7] The nonbiotinylated GP5+ strands of the nested HPV amplicons were digested by incubation for 30 minutes at 37°C with T7 gene 6 exonuclease at 0.4 unit/μL (New England Biolabs), leaving the single-stranded biotinylated GP6+ strands intact. The GP6+ strands were then hybridized to a mixture of 45 sets of Luminex Xmap microspheres linked to 30-mer oligonucleotides specific for the 45 types of mucosal HPV. Hybrids were labeled with a 0.04-mg/μL solution of streptavidin-phycoerythrin in 1.5× tetramethylammonium chloride (Sigma), and the samples were analyzed on a LiquiChip workstation (Qiagen) at 60°C. LiquiChip is a flow cytometer that sorts the sets of microspheres on the basis of their differential staining with two fluorophores. LiquiChip also measures the phycoerythrin fluorescence of the microspheres conjugated with the amplified HPV DNA.

Data entry and analysis

Data entry was completed with Epi Info version 3.3.2 (Centers for Disease Control and Prevention, Atlanta, Georgia, United States). Double data entry was used to validate the data entry process. The two data sets were compared by using the Data Compare utility and corrections were made by referring to the original survey instrument.

Descriptive data analysis was performed using Epi Info version 3.3.2. This process involved producing frequency tables for categorical variables and simple measures of central tendency and dispersion for continuous variables.

Data manipulations and subsequent analyses were performed using SPSS 15.0 (SPSS for Windows, release 15.0.0, 2006, SPSS Inc., Chicago, Illinois, United States). Participants with HPV-positive samples were grouped into high-risk, low-risk, and unknown-risk groups, according to the epidemiologic classification by Muñoz et al. (5), as follows:

- High risk if at least one high-risk HPV genotype (HPV types 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, and 82) was detected in the sample, regardless of the presence of low-risk genotypes or HPV genotypes of unknown risk;
- Low risk if no high-risk HPV genotypes were detected but at least one low-risk HPV genotype (HPV types 6, 11, 40, 42, 43, 44, 54, 61, 70, 72, and 81) was detected, regardless of the presence of genotypes of unknown risk; and
- Unknown risk if, in such samples, the genotype(s) detected was (were) of unknown risk (HPV types 13, 30, 32, 34, 62, 67, 69, 71, 74, 83, 84, 85, 86, 87, 89, 90, and 91).

Cross-tabulations were then conducted to assess the relationship between the HPV status of participants—HPV high risk, HPV low risk, HPV unknown risk, and HPV negative—and other variables of interest. This grouping was collapsed into HPV-positive cases (HPV high risk, HPV low risk, and HPV unknown risk) versus HPV-negative cases and the cross-tabulation analysis was repeated. Finally, the analysis was repeated by grouping samples into HPV high risk versus other (HPV low risk, HPV unknown risk, and HPV negative). Chi-square analyses were run on all cross-tabulations with a 5% level of significance.

RESULTS

Characteristics of the study cohort

The study sample consisted of a cohort of 310 sexually active women between the ages of 18 and 65 years (mean age 34.9 years). The demographic profile of the cohort is shown in Table 1. Risk factors associated with HPV infection are presented in Table 2.

Pap smear and HPV test results

Of the 310 smears done, 294 smears were satisfactory for analysis; 279 (94.9%) of them had normal cytology. Fifteen women [5.1%, 95% confidence interval (CI) 3.0%–8.1%] had abnormal cytology. In 3 of these women (20.0%, 95% CI 5.4%–45.4%) the abnormal cytology was classified as atypical squamous cells of unknown significance (ASCUS), in 11 (73.3%, 95% CI 47.5%–90.9%) it was classified as low-grade squamous intraepithelial lesions, and in 1 (6.7%, 95%

TABLE 1. Demographic characteristics of 310 female participants in a study of HPV genotypes and their prevalence in Trinidad, 2007

Variable[a]	No.	%
Marital status		
Single	122	39.4
Married	99	31.9
Other	89	28.7
Employment status		
Employed	177	57.1
Unemployed	133	42.9
Gross household income (monthly)		
< 5 000 TT dollars (US$800)	128	41.3
> 5 000 TT dollars (US$800)	175	56.5
Education		
Primary or less	56	18.1
Secondary only	182	58.7
Tertiary	53	17.1
Other	17	5.5
Ethnicity[b]		
Mixed	142	45.8
Afro-Caribbean	113	36.5
Indo-Caribbean	52	16.8

Note: HPV: human papillomavirus, TT: Trinidad and Tobago. Nonresponses are not included.

[a] Details of the age distribution are shown in Figure 1.

[b] Values for the general female population are 21.6% mixed, 35.3% Afro-Caribbean, 41.2% Indo-Caribbean (Central Statistical Office, Ministry of Planning and Development, Government of Trinidad and Tobago, 2000 census).

[7] Goleski et al. 2008, US Provisional Patent Application 61/296,245.

TABLE 2. Risk factors associated with women who are HPV positive[a] among a cohort of women in Trinidad, 2007

Risk factor	Frequency		Chi square[b]	*P*
	No.	%		
Use of cigarettes or cigars in past 12 months[c]				
Yes	14	11.1	0.18	0.671
No	110	87.3		
Initiation of sexual activity				
< 15 years of age	14	11.1	0.14	0.711
> 15 years of age	112	88.8		
Number of sexual partners				
1 or 2	41	32.5	3.91	0.048[d]
3 ≥	85	65.1		
Contraceptive use[c]				
No	50	39.7	4.91	0.027[d]
Yes	73	57.9		
History of sexually transmitted infection[c]				
Yes	10	7.9	0.08	0.796
No	114	90.5		
Family history of cervical cancer[c]				
Yes	12	9.5	1.32	0.251
No	111	88.1		
Number of pregnancies				
1 or 2	84	66.7	10.15	0.001[d]
3 ≥	42	33.3		
Number of live births[c]				
1 or 2	44	34.9	0.22	0.636
3 ≥	34	27.0		
Previous Pap smear				
Never	54	42.9	6.01	0.014[d]
Ever	72	57.1		

Note: HPV: human papillomavirus, Pap: Papanicolaou.
[a] $n = 126$.
[b] Pearson's chi square used to assess significant association between risk factor and having tested positive for HPV.
[c] Totals do not equal 126 due to nonresponses.
[d] $P < 0.05$.

TABLE 3. Frequency of occurrence of HPV genotypes, organized into risk group, among HPV-positive samples from 310 female participants in a study of HPV genotypes and their prevalence in Trinidad, 2007

Genotype	Frequency	
	No.	%[a]
High risk		
HPV 52	16	12.7
HPV 66	13	10.3
HPV 16	12	9.5
HPV 18	11	8.6
HPV 58	10	7.9
HPV 33	6	4.0
HPV 31	5	3.3
HPV 53	5	3.3
HPV 45	3	2.0
HPV 51	3	2.0
HPV 59	3	2.0
HPV 35	2	1.3
HPV 73	2	1.3
HPV 39	1	0.6
HPV 56	1	0.6
HPV 82	1	0.6
Low risk		
HPV 54	8	5.2
HPV 42	5	3.3
HPV 61	4	2.6
HPV 72	4	2.6
HPV 6	3	2.0
HPV 81	3	2.0
HPV 40	2	1.3
HPV 70	2	1.3
HPV 11	1	0.6
HPV 44	1	0.6
Unknown risk		
HPV 62	12	9.5
HPV 83	8	5.2
HPV 84	6	4.0
HPV 32	3	2.0
HPV 69	3	2.0
HPV 67	2	1.3
HPV 85	2	1.3
HPV 86	2	1.3
HPV 30	1	0.6
HPV 71	1	0.6
HPV 74	1	0.6
HPV 91	1	0.6

Note: HPV: human papillomavirus.
[a] Expressed as percentage of the number of HPV-positive samples (126/310). More than one genotype may have been present in one sample.

CI 0.3%–28.7%) it was classified as high-grade squamous intraepithelial lesions (HSIL) using the Bethesda System for reporting cervical cytology.

HPV amplification by PCR gave an overall prevalence of HPV infection of 40.6% (126/310, 95% CI 35.3%–46.2%), including all HPV risk types; 65.9% (83/126, 95% CI 57.3%–73.8%) of these infections were identified as high-risk HPV genotypes, 12.7% (16/126, 95% CI 7.7%–19.4%) were low-risk HPV types, and 21.4% (27/126, 95% CI 14.9%–29.2%) were identified as being HPV types of unknown risk.

Relative occurrence of high-risk HPV genotypes

A total of 38 HPV genotypes, including 16 high-risk HPV genotypes, were detected in the study sample. The most frequently occurring high-risk HPV genotype was HPV 52 (12.7%, 95% CI 7.7%–19.4%), followed by HPV 66 (10.3%, 95% CI 5.9%–16.6%), HPV 16 (9.5%, 95% CI 5.3%–15.6%), HPV 18 (8.7%, 95% CI 4.7%–14.7%), and HPV 58 (7.9%, 95% CI 4.1%–13.7%), as shown in Table 3.

The frequencies of infections with HPV types of low and unknown risk were comparatively smaller than the occurrence of high-risk HPV infections (Table 3). Of the 29 HPV low-risk infections identified, 12 were found only as coinfections with the other risk groups and 11 of the 34 infections of unknown risk were also found only as coinfections with other HPV types. Thirty-eight (30.2%, 95% CI 22.6%–38.6%) of the HPV-infected women were infected with multiple types at the time of sampling.

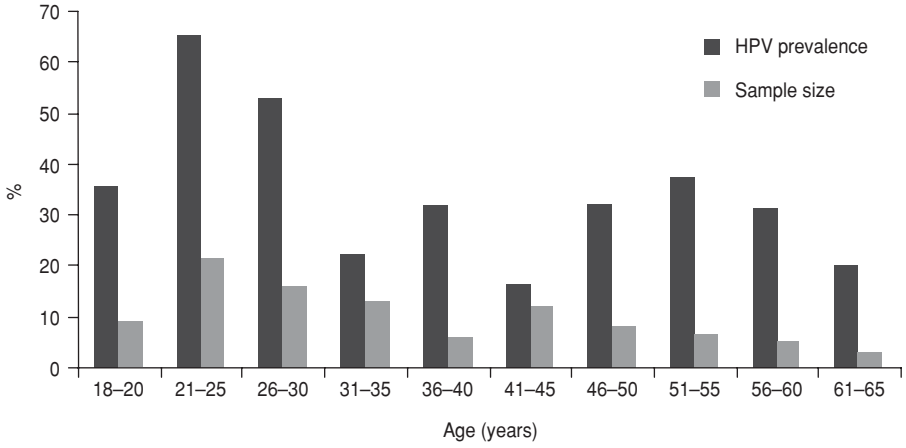
HPV infection and age distribution

The age distribution of women who were HPV positive is shown in Figure 1. The highest prevalence of HPV infection was observed among women aged < 30 years (63.0%), with a peak in the 21- to 25-year age group. There was a significant difference in the rate of HPV infection between women aged < 30 years and those ≥ 30 years (24.6%, $P < 0.0001$). However, prevalence remained high in the older age groups, ranging between 16.2% and 37.5% (Figure 1).

HPV genotypes and cytologic abnormalities

High-risk HPV 16 was found in 3 (20.0%, 95% CI 5.4%–45.4%) and HPV 18 in 1 (6.6%, 95% CI 0.3%–28.7%) of the 15 women in the sample with abnormal cytology. The other high-risk types occurring with abnormal cytology were HPV 66 (3/15); HPV 31 (1/15); HPV 51 (1/15);

FIGURE 1. Sample size, as percentage of total study cohort and HPV prevalence, within age groups, among a cohort of 310 women in a study of HPV genotypes and their prevalence in Trinidad, 2007



HPV = human papillomavirus.

HPV 52 (1/15); HPV 45, HPV 53, and HPV 59 (1/15) as a triple infection; HPV 58 (1/15) with HPV 16 as a coinfection; and HPV 82 (1/15) with HPV 66 as a coinfection. There were also three women with abnormal cytology classified as ASCUS in which no high-risk HPV type was identified. Those women were infected with low-risk types HPV 61 and HPV 81 and one type of unknown-risk HPV 83, respectively, in single infections.

HPV infection and associated risk factors

In this study, the risk factors that were found to be positively associated (at the 5% level of significance) with HPV infection were lack of use of contraceptives, three or more pregnancies, not having had a Pap smear, and having three or more sexual partners (Table 2).

DISCUSSION

In this study, we determined the prevalence of HPV infections and evaluated the frequency of HPV genotypes in a sample of cancer-free women from Trinidad, median age 34.9 years. The prevalence of HPV within the study sample was high (40.6%) with the majority (60.0%) of infections being high-risk HPV infections. This finding is consistent with the findings of similar studies in two other Caribbean islands: Tobago, the sister island of the twin-island state of Trinidad and Tobago (7), and Jamaica (12), which reported HPV prevalences of 35.4% and 87.5%, respectively, and high-risk HPV infections as 57.3% and 60.9% of all infections, respectively.

Infections with multiple genotypes of HPV were common among the study sample, with more than one HPV genotype being identified in 30.0% of infections. Similarly, high rates of mixed HPV infections were also found in Tobago (7) and Jamaica (12): 33.0% and 60.9%, respectively. This finding is consistent with a previous report that multiple high-risk HPV infections are common in young women with normal cytology (13).

A cohort study designed to assess the relationship between the cumulative and concurrent number of HPV types in any grade of squamous intraepithelial lesions and HSIL with multiple HPV infections showed that the HPV types seem to act synergistically in cervical carcinogenesis (14). It is noteworthy that the Pan American Health Organization has reported cervical cancer as the leading cause of cancer deaths among women in Latin America and the Caribbean (15). It has also been reported that the cervical cancer incidence rate in Trinidad and Tobago is about two times higher than the worldwide rate (7). It remains to be established whether the high prevalence of multiple HPV coinfections and the large proportion of high-risk HPV infections observed in this study are reflective of the nationwide situation and hence act as major contributors to the high incidence of cervical cancer in Trinidad and Tobago.

The study sample was characterized by a high degree of heterogeneity of HPV types, with 38 HPV types being detected. This finding represents one of the highest levels of heterogeneity of HPV types reported for any study population and may reflect the strength of the HPV genotyping methodology used. It appears that, for populations with very high HPV prevalence, which most often are resource-poor populations (16), there is an increased likelihood of very high HPV genotype heterogeneity, so that the most comprehensive tools must be used when investigating HPV genotype distribution within these populations.

The Luminex method used in this study detects and recognizes 45 mucosal HPV types without cross-hybridization, even in the presence of multiple infections. The Tobago study (7) used a combination of DNA sequencing and the Roche linear array HPV genotyping test, which is able to detect 37 genotypes, and detected 32 genotypes in the study sample. The Jamaica study (12) also used the Roche system and detected 36 genotypes. In comparison, populations reporting low HPV prevalence also seem to display low HPV heterogeneity. A study comparing HPV genotype distribution in cervical carcinomas from Suriname, a high-incidence country, and the Netherlands, a low-incidence country, detected 13 HPV genotypes in carcinomas from the Surinamese group compared with only 9 genotypes in the Dutch group (17).

The most frequent high-risk types found in the current study were HPV 52 (12.7%), HPV 66 (10.3%), HPV 16 (9.5%), HPV 18 (8.7%), and HPV 58 (7.9%). Other high-risk HPV types detected were types 31, 33, 39, 45, 51, 53, 56, 59, 73, and 82. Many surveys, including a worldwide study on the distribution of HPV types in women with normal cytology (16, 18), have indicated that the most common HPV type in single or multiple infections is HPV 16. The latter report (18) also found that HPV 16, HPV 18, HPV 31, HPV 58, and HPV 52 are the five most common HPV types in HPV-positive women worldwide; however, there were variations in the prevalence estimates for the different types. The five most common HPV types of the current study—HPV 52, HPV 66, HPV 16, HPV 18, and HPV 58—matched the worldwide pattern fairly well, except for the notable high prevalence of HPV 66, which was the second most common high-risk HPV type. In the study conducted in Tobago, HPV 66 was also the second most common high-risk type (7);

however, both studies showed differences in the prevalence estimates for the high-risk HPV types. The most common high-risk cervical HPV type detected in the Tobago study was HPV 45, with the five most common types reported as HPV 45, HPV 66, HPV 16, HPV 35, and HPV 52, in that order. The factors contributing to the differences between the studies warrant investigation. These factors could include differences in population demographics (the Tobago population is predominantly of African descent, while in Trinidad 37.5% of the population is of African descent and 40.0% is of southern Asian descent) and the impact of a differential tourism industry; tourism is the primary industry in Tobago, but its contribution is relatively minor in Trinidad. In the Jamaica study, HPV 45 and HPV 58 were more prevalent than HPV 16 and HPV 18 (12). The findings from all three studies of Caribbean cohorts therefore show a deviation from the accepted norm of HPV 16 and HPV 18 being the most prevalent high-risk HPV types.

Regional heterogeneity decreases with increasing severity of cervical lesions, with HPV 16 becoming increasingly dominant in such cases (16, 19). For example, HPV 16 prevalences in women with HSILs were 32.0%, 37.0%, and 53.0% in Africa, South America, and Europe, respectively; for squamous cell carcinoma, prevalences were 50.0%, 52.0%, and 62.0%, respectively (16). A study in Mozambique reported that, whereas HPV 51 and HPV 35 were the most common in a cohort of cytologically normal women, HPV 16 and HPV 18 were the most frequently identified types in cervical cancer tissue (20).

In this study, 3 of the infections in the 15 women with abnormal cytology were associated with HPV 16 and 1 was associated with HPV 18. Other HPV types in women with abnormal cytology included types 31, 45, 52, 53, 58, 59, 66, 73, and 82. The only woman identified with HSIL in the study was associated with multiple HPV infections with high-risk HPV 66 and low-risk HPV 61 and HPV 62. However, with only 15 specimens giving abnormal cytologic readings, the types of HPV most associated with cytologic changes in the general population cannot be inferred. Larger studies are needed to assess the prevalence of HPV 16 and HPV 18 in high-grade abnormalities and cancer in order to assess the potential effectiveness of an HPV immunization program in Trinidad and Tobago.

The present study is in agreement with previous findings that HPV infection is more common among women below the age of 30 years, decreasing in older women, and supports the position that HPV is a common sexually transmitted infection (18). In the current study, however, HPV prevalence remained high in those above 30 years of age, which is similar to the situation reported for African countries (18). This study suggests that, as with African populations, women in Trinidad are less likely to be screened for cervical cancer. A third of the study population had never been screened and less than 40.0% of participants accessed regular Pap screening services. This poor rate of screening, together with the high prevalence of cervical HPV infections within the study sample, is a worrying situation and suggests the need for urgent screening and education of the wider population.

Results from other studies of HPV cofactors suggest that sexual behavior, multiparity (pregnancies ≥ 3), contraceptive use, and cigarette smoking are HPV cofactors related to the development of cervical cancer (21). In this study, the factors found to be significantly associated with HPV infection were lack of use of contraceptives, three or more pregnancies, not having had a Pap smear, and having three or more sexual partners. These results may have been influenced by the small sample size and need to be confirmed in a larger population-based study along with the other risk factors, which were not identified as associated with HPV infection in this study.

The main limitation of this study is that a convenient sample was used. A consequence of this limitation is that the results of the study cannot be generalized to the female population of Trinidad. Of note are the differences in ethnic composition of the study cohort (mixed 45.8%, Afro-Caribbean 36.5%, Indo-Caribbean 16.8%) and that of the general female population (mixed 21.6%, Afro-Caribbean 35.3%, Indo-Caribbean 41.2%).[8] Voluntary participation could have resulted in a bias toward participants who believed they were at risk of infection and so led to bias in the prevalence estimates for HPV infection. Furthermore, the data collected through the interviewer-administered questionnaire were self-reported and so may have been influenced by recall bias.

In conclusion, the prevalence of cervical HPV, and notably of high-risk HPV infections, was high in a convenience sample of 310 cancer-free, sexually active women from Trinidad, representing a mixture of demographic indicators for age, ethnicity, social status, and lifestyle choices. In spite of the high incidence of cervical cancer in Trinidad and Tobago, few of the women studied had ever accessed Pap smear screening. The cervical HPV profile was markedly heterogeneous, with 16 high-risk HPV genotypes identified among the 126 women with cervical HPV infections. Currently, nothing is known about the relative contribution of each of the 16 high-risk genotypes to the progression of cervical cancer in Trinidad or about their association with disease presentation and severity. It is recommended that the study be extended to a larger representative cohort to determine whether the findings hold true for the general population. The high-risk HPV genotypes contributing most to the development of invasive cervical cancers in Trinidad should be determined to assess the public health impact of each of the high-risk genotypes detected in the study and to establish the usefulness of including prophylactic HPV vaccination in the national schedule of immunization. Strengthening the screening programs for the prevention and control of cervical cancer is also recommended.

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[8] Central Statistical Office, Ministry of Planning and Development, Government of Trinidad and Tobago, 2000 census data.

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RESUMEN

Genotipos del papilomavirus humano y su prevalencia en una cohorte de mujeres en Trinidad

Objetivo. Se determinaron los genotipos del papilomavirus humano (PVH) y su prevalencia relativa en una cohorte de 310 mujeres sexualmente activas de Trinidad, en la zona de las Indias Occidentales.

Métodos. Se tomaron muestras del cuello uterino con espátula de Ayre y cepillo endocervical. Las muestras se usaron para llevar a cabo la prueba convencional de Papanicolaou y para determinar los genotipos de PVH mediante la amplificación de una sección del gen vírico L1, seguida de secuenciación del ADN e hibridación con sonda.

Resultados. Se encontró una infección por PVH en 126 de las 310 mujeres (40,6%). De ellas, 83 (65,8%) estaban infectadas con PVH de alto riesgo, 16 (12,7%) con PVH de bajo riesgo, y 27 (21,4%) con tipos de PVH de riesgo desconocido. De los PVH de alto riesgo, el más frecuente fue el PVH 52 (12,7%), seguido por el PVH 66 (10,3%), el PVH 16 (9,5%) y el PVH 18 (8,6%). Entre las 15 mujeres con citología anormal se encontraron los PVH de alto riesgo 16 y 66 en 3 (20,0%) mujeres cada uno, y el PVH 18 en 1 (6,6%).

Conclusiones. Tanto la prevalencia de PVH en el cuello uterino como la heterogeneidad de los genotipos de PVH son elevadas en esta cohorte de Trinidad. La importancia relativa de los genotipos de PVH en la aparición de las lesiones cervicales requiere de mayor investigación en Trinidad para conocer más a fondo las características epidemiológicas de las infecciones por PVH, así como para determinar el papel del estudio de los PVH en la detección sistemática, la prevención y el control del cáncer del cuello uterino. Este estudio piloto suministró información importante sobre la prevalencia de los genotipos de PVH, que se usará en futuros estudios que se lleven a cabo en todo el país.

Palabras clave Prevención de cáncer de cuello uterino; papillomaviridae; prevalencia; Caribe; Trinidad y Tobago.