Sociodemographic characteristics and sexual behavior as risk factors for human papillomavirus infection in Saudi Arabia

F.S. Alhamlan a,b, H.H. Khayat a, S. Ramisetty-Mikler b,c, T.A. Al-Muammar d, A.M. Tulbah e, I.A. Al-Badawi f, W.I. Kurdi f, M.I. Tulbah f, A.A. Alkhenizan d, A.N. Hussain d, M. Ahmed d, M.N. Al-Ahdal a,b,c,*

* Corresponding author. Tel.: +966 11 442 7867; fax: +966 11 442 4519. E-mail address: ahdal@kfshrc.edu.sa (M.N. Al-Ahdal).

** Article history:
Received 24 December 2015
Received in revised form 31 March 2016
Accepted 3 April 2016

** Corresponding Editor: Eskild Petersen, Aarhus, Denmark.

** Keywords:
Human papillomavirus
HPV
Epidemiology
Sociodemographic characteristics
Saudi Arabia

** Summary
Objectives: To determine the prevalence and the sociodemographic characteristics and sexual behavior risk factors for human papillomavirus (HPV) infection in a hospital-based cohort of women in Saudi Arabia.

Methods: Cervical specimens and questionnaire data were collected from women attending clinics in Riyadh, Saudi Arabia. Cervical specimens were examined for abnormal cytology using a standard Pap test and for the presence of HPV-DNA using PCR and reverse line blot hybridization tests.

Results: Approximately 73% of the 400 women tested were Saudi nationals. Nearly 50% were under 40 years old (range 22–80 years, mean ± standard deviation 41.20 ± 10.43 years). Approximately 17% of the women were HPV-positive. The most commonly detected HPV types were HPV-18 (34%) and HPV-16 (19%), with multiple infections detected in 10% of positive specimens. Multivariate analyses revealed that smoking and multiple partners were significant risk factors for HPV infection (p < 0.01).

Conclusions: Because of societal challenges and an unsubstantiated assumption of low HPV prevalence, few studies have examined sociodemographic characteristics or sexual behaviors associated with HPV in Saudi women. However, a high prevalence of HPV infection was found, with smoking and multiple partners as significant risk factors, in this hospital-based cohort of predominantly Saudi women.

© 2016 The Authors. Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

The presence of human papillomavirus (HPV) infection, a key etiological factor in carcinoma of the cervix and other mucosal epithelia, is associated with approximately 4.8% of all human cancers, posing a significant morbidity and mortality risk worldwide. Papillomaviruses belong to a family of small, non-enveloped viruses with a double-stranded DNA genome of approximately 7.9 kb.8 HPV establishes productive infections only in keratinocytes of the skin or mucous membranes. More than 180 genotypes of HPV have been sequenced, and these are classified as either low-risk HPV (LR-HPV) or high-risk HPV (HR-HPV), depending on their oncological potential for transforming cells. Benign hyperproliferative lesions or genital warts are caused by LR-HPVs, while HR-HPVs are strongly associated with premalignant and malignant cervical lesions that lead to different types of cancers such as cervical, vulvar, vaginal, penile, oropharyngeal, and anal cancers.3,4

Cervical cancer is the eighth most frequent cancer among women in Saudi Arabia aged 15 to 44 years,5 and according to the World Health Organization, 6.51 million Saudi women 15 years and older are at risk of developing cervical cancer.6 An estimated 152 Saudi women are diagnosed with cervical cancer and 55 die from the disease every year. By contrast, the prevalence of HPV in Saudi Arabia and many developing countries remains unknown or controversial. However, approximately 2.2% of women living in...
Western Asia, which includes Saudi Arabia, harbor cervical HPV infection, with approximately 68.5% of invasive cervical cancers in Asia attributable to HPV-16 or HPV-18. In Saudi Arabia, the prevalence of HPV infection is under debate. Some researchers have suggested that Saudi Arabia has the lowest HPV infection rate in the world (e.g., 1.9 cases/100,000 women), but others claim a much higher rate.

Cervical cancer is preventable, and with an early diagnosis, it may also be curable. Unfortunately, most women in developing countries, including Saudi Arabia, remain undiagnosed until advanced stages, which decreases survival rates. Therefore, the present study was conducted to report the prevalence of HPV infection in a hospital-based cohort of women in Saudi Arabia and to establish a sociodemographic profile and sexual health behavior as risk factors for HPV infection.

2. Materials and methods

2.1. Participants, specimens, and data collection

Women who attended the Primary Care Clinic (namely, Family Medicine) or the Obstetrics and Gynecology Clinic at King Faisal Specialist Hospital and Research Centre (KFSHRC) in Riyadh, Saudi Arabia, for routine cervical examinations from November 2013 to November 2015 were included in this 2-year study. These clinics treat persons of all socioeconomic classes who are eligible for treatment in this hospital. The inclusion criteria for participation in the study were women who were married, divorced, or widowed, and the exclusion criteria were women who were pregnant or virgin. Given religious and cultural constraints, Saudi women who have never married could not be recruited for this study; therefore, all women who had never married were excluded from the study to avoid bias. Women who did not fill in the questionnaire in its entirety were also excluded from the study; thus, all survey questions were answered.

Cervical specimens were collected using a cytobrush. Two cytobrushes were used to collect the specimens: the first was transferred into a vial containing liquid-based cytology transport medium (PreservCyt; ThinPrep Pap Test Boxborough, MA, USA) for use in a routine Papanicolaou (Pap) test; the second cytobrush was transferred into a vial containing RNA later stabilizing reagent (Qiagen, Valencia, CA, USA) for use in molecular detection experiments. The cervical specimens were examined for normal or abnormal cytology, and the stages of abnormal cytology were identified according to the Bethesda classification, as follows: negative for intraepithelial lesion (NIL), atypical squamous cells of undetermined significance (ASCUS), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL), and cervical carcinoma.

Questionnaires were completed by the enrolled participants and were collected by a clinical coordinator during the participants’ clinical visits. Women who agreed to participate in the study filled out the questionnaire in its entirety, leaving no question unanswered.

2.2. Ethics approval

This study was approved by the Office of Research Affairs (ORA) of King Faisal Specialist Hospital and Research Centre (RAC #2130 033), and written informed consent was obtained from each participant.

2.3. DNA extraction from cervical specimens

Cervical cells were collected using centrifugation, and total genomic DNA was extracted using a Gentra Puregene Cell Kit according to the manufacturer’s instructions (Qiagen, Hilden, Germany). The extracted DNA was eluted in 50 μl of RNase/DNase-free water. The quality and quantity of the extracted DNA were determined using a NanoDrop spectrophotometer (NanoDrop Technologies, Wilmington, DE, USA). The quality of DNA extracted from cervical specimens was determined with β-globin primers. The amplified products were visualized using 1% agarose gels stained with ethidium bromide.

2.4. HPV detection

The MY09/MY11 and GP5+/GP6+ primer sets were used to target sequences located within the L1 region. The MY09/11 primer set targeted a 450-bp conserved sequence and was used for the first round of PCR. The GP5+/GP6+ primer set targeted a 150-bp sequence within the 450-bp product and was, therefore, used for nested PCR. The internal control was the β-globin gene, the positive controls were HeLa and SiHa cells, and the negative controls were UltraPure DNase/RNase-free water and HEK293 cells. Positive amplicons were sequenced for confirmation at the Sequencing Core Facility of KFSHRC using an ABI3730XL sequencer (Applied Biosystems, Foster City, CA, USA).

2.5. Genotyping by reverse line blot (RLB) hybridization

The oligoprobes (n = 23; C12 Aminolink) were synthesized as described previously. The genotyping protocol followed has been published previously. Briefly, oligoprobes were spotted on a carboxyl-coated nylon membrane (Biodyne C 0.45 μm; Pall Corporation, Pensacola, FL, USA). For hybridization, biotinylated PCR products were added to the membrane. Subsequently, the membrane was incubated with an anti-fluorescein peroxidase conjugate. HPV genotypes were detected using an enhanced chemiluminescence kit.

2.6. Data and statistical analyses

Demographic information and sexual behavior data were collected using a questionnaire provided to each participant. Previously published papers were used to identify the risk factor variables used in the present study. The demographic variables included age, religion, marital status, education, nationality, smoking habit, and income. The sexual variables included age at first intercourse, number of sexual partners, number of children, contraceptive use, and duration and type of contraception used.

All data collected were stored and analyzed using IBM SPSS Statistics version 22 software (IBM Corp., Armonk, NY, USA). Univariate and descriptive statistics were used to estimate the proportions. Significant associations between HPV status and study variables were assessed using a Chi-square test. Logistic regression modeling was used to determine the adjusted odds ratios and 95% confidence intervals (95% CI) to estimate the relative odds for demographic and sexual behavior variables and smoking status. Variables that were significant in univariate analyses and variables that were considered relevant based on the previous research were evaluated in a multiple logistic regression model. The final model was created with the inclusion of some risk variables with potential biological significance, which were those that remained statistically significant after adjustment. All p-values reported were two-sided and were considered to be statistically significant at p < 0.05.

3. Results

3.1. HPV prevalence and cytology results

Of the 400 women who were recruited and examined in this study, approximately 17% (n = 67) tested positive for HPV DNA. The
most commonly detected HPV types were HPV-18 (32%, n = 21) and HPV-16 (21%, n = 14), followed by HPV-11 (14%, n = 9), HPV-31 (7.6%, n = 5), HPV-58 (4%, n = 3), HPV-56 (3%, n = 2), and HPV-42 (3%, n = 2). Multiple infections were detected in 10% (n = 7). The results of the cytology analysis showed that 93% (n = 368) of the samples were normal (i.e., NIEL), 2% (n = 8) were ASCUS, 3% (n = 12) were LGSIL, 0.75% (n = 3) were HGSIL, and 0.25% (n = 1) were cervical cancer. Eleven cervical samples were β-globin-negative and were excluded from the study. HPV-18 was detected in NIEL, HGSIL, and cancer samples, HPV-16 was detected in NIEL, ASCUS, LGSIL, and HGSIL, and HPV-56 was detected in NIEL and ASCUS. Multiple infections were detected in NIEL, ASCUS, and LGSIL (Figure 1).

The HPV genotype prevalence stratified by age revealed a number of significant findings. First, HPV types varied in women younger than 40 years old compared with those older than 40 years, and declined significantly in women >50 years. HPV-11 infection was most prevalent in the 20–29 years age group, HPV-16 in those aged 40–49 years, and HPV-18 in women aged ≥50 years. Multiple infections were most prevalent in women younger than 40 years of age (Figure 2).

### 3.2. Demographic characteristics

A total of 400 women aged 22–80 years were tested for HPV. Approximately 50% (n = 195) of the women were under the age of 40 years, with a mean age of 41.20 years (standard deviation (SD) 10.43, 95% CI 40.17–42.22). Most of the women were from Saudi Arabia (73%, n = 291), followed by the Philippines (7.3%, n = 29) and Jordan (4.0%, n = 16), with a small percentage (<2%) from Europe, the Americas, Africa, and South Asia. Nearly 90% (n = 357) of the women were Muslim, and the remainder were Christians. Most had a higher level of education (45%, n = 181), with 37% (n = 149) reporting a secondary school education, 10% (n = 41) an intermediate school education, and 7% (n = 28) a primary school education.

Approximately 40% (n = 158) of these women were in households with monthly incomes of 5333 USD or more. The monthly household income was 2666–5333 USD for 40% (n = 161), 1066–2400 USD for 8% (n = 31), and less than 800 USD for 8.5% (n = 34). Four percent (n = 16) reported having no income. Most of the women (87.5%; n = 350) were married, with the remaining either divorced or widowed. Close to one in three women (30%; n = 119) reported smoking cigarettes. Table 1 presents these finding and shows sociodemographic data according to HPV status.

Bivariate analyses indicated that only smoking was associated with HPV status. Compared with non-smokers (12.5%), a higher percentage of smokers (27%) tested positive for HPV (Chi-square = 12.5, p < 0.0001). The results of a multivariate logistic regression analysis, after controlling for the confounders of age, education, and employment, indicated that women who smoked had approximately 2.5 times higher odds of testing positive for HPV (Supplementary Material, Table S1).

### 3.3. Sexual behaviors

The mean age at first sexual intercourse was 21.5 years (SD 5.0, range 11–38 years), with approximately half (51%) having experienced sexual intercourse by the age of 20 years. Overall, 88% of the women reported having a single sexual partner, and the remaining women (approximately 12%) reported more than one sexual partner in their lifetime. Approximately 8% had no children. Among those who reported having children, the average number of children was 5.0 (SD 2.5, range 1–15) (Table 2).

HPV positivity was higher in women with three or more lifetime sexual partners (44%) compared with women who had one partner (16%). Odds ratios increased with increasing numbers of lifetime sexual partners (Supplementary Material, Table S1).

Most women (72%, n = 287) reported using some type of contraception in their lifetime. Among them, the intrauterine device (IUD) (61%) and birth control pills (37%) were the two

---

**Figure 1.** HPV genotypes and cytology results. The most commonly detected HPV types were HPV-18 (34%) and HPV-16 (19%), followed by HPV-11 (13%), HPV-31 (6%), HPV-58 (3%), HPV-56 (3%), and HPV-42 (3%). HPV-18 was detected in NIEL, HGSIL, and cancer samples. HPV-16 was detected in NIEL, ASCUS, LGSIL, and HGSIL samples. HPV-56 was detected in NIEL and ASCUS samples. Multiple infections were detected in NIEL, ASCUS, and LGSIL samples.
Condoms were used by only a few (1.7%). The average duration of contraception use reported was 4 years (SD 3.2 years), with a maximum use of 25 years (Table 2).

Table 2 presents sexual behavior data according to HPV status. Bivariate analyses indicated that among sexual behavior variables, only the number of sexual partners was significantly associated with HPV status (Chi-square = 8.8, p < 0.01).

---

**Figure 2.** HPV genotypes and age categories. Multiple infections were highest in the youngest population. HPV-18 was most prevalent among women ≥50 years old, whereas HPV-16 was most prevalent among 40–49-year-olds and HPV-11 infection was most prevalent in those aged 20–29 years.

**Table 1**

Sociodemographic characteristics of the study cohort

<table>
<thead>
<tr>
<th>Table 1</th>
<th>HPV-positive 16.8% (n=67)</th>
<th>HPV-negative 83.3% (n=377)</th>
<th>Total % (N=400)</th>
<th>Chi-square (df)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>% (n)</td>
<td>% (n)</td>
<td>% (n)</td>
<td>5.8 (4)</td>
</tr>
<tr>
<td>20–29 (n=65)</td>
<td>20.0 (13)</td>
<td>80.0 (52)</td>
<td>16.3 (65)</td>
<td></td>
</tr>
<tr>
<td>30–39 (n=119)</td>
<td>17.0 (20)</td>
<td>83.0 (99)</td>
<td>30.0 (119)</td>
<td></td>
</tr>
<tr>
<td>40–49 (n=123)</td>
<td>17.0 (21)</td>
<td>83.0 (102)</td>
<td>31.0 (123)</td>
<td></td>
</tr>
<tr>
<td>50+ (n=93)</td>
<td>13.0 (13)</td>
<td>86.0 (80)</td>
<td>23.7 (93)</td>
<td></td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>40.3 (10.67)</td>
<td>41.43 (10.38)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Religion</td>
<td>25.6 (11)</td>
<td>74.4 (32)</td>
<td>11.0 (43)</td>
<td></td>
</tr>
<tr>
<td>Christian (n=43)</td>
<td>16.0 (56)</td>
<td>84.0 (301)</td>
<td>89.0 (357)</td>
<td></td>
</tr>
<tr>
<td>Muslim (n=357)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nationality</td>
<td>16.0 (47)</td>
<td>84.0 (244)</td>
<td>73.0 (291)</td>
<td></td>
</tr>
<tr>
<td>Saudi (n=291)</td>
<td>18.0 (20)</td>
<td>82.0 (89)</td>
<td>27.0 (109)</td>
<td></td>
</tr>
<tr>
<td>Non-Saudi (n=109)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>11.0 (3)</td>
<td>89.0 (25)</td>
<td>7.0 (28)</td>
<td></td>
</tr>
<tr>
<td>Primary (n=28)</td>
<td>19.5 (8)</td>
<td>80.5 (33)</td>
<td>10.0 (41)</td>
<td></td>
</tr>
<tr>
<td>Intermediate (n=41)</td>
<td>19.0 (28)</td>
<td>81.0 (121)</td>
<td>37.0 (149)</td>
<td></td>
</tr>
<tr>
<td>Secondary (n=149)</td>
<td>15.5 (28)</td>
<td>84.5 (153)</td>
<td>45.0 (181)</td>
<td></td>
</tr>
<tr>
<td>Higher (n=181)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annual household income (USD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;800.01 (n=34)</td>
<td>20.0 (10)</td>
<td>71.0 (24)</td>
<td>9.0 (34)</td>
<td>4.1 (3)</td>
</tr>
<tr>
<td>1066.68–2400.03 (n=31)</td>
<td>13.0 (4)</td>
<td>87.0 (27)</td>
<td>8.0 (31)</td>
<td></td>
</tr>
<tr>
<td>2666.70–5333.40 (n=161)</td>
<td>16.0 (26)</td>
<td>(84.0 (135)</td>
<td>42.0 (161)</td>
<td></td>
</tr>
<tr>
<td>&gt;5333.40 (n=158)</td>
<td>17.0 (27)</td>
<td>83.0 (131)</td>
<td>41.0 (158)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married (n=350)</td>
<td>16.3 (57)</td>
<td>83.7 (293)</td>
<td>87.5 (350)</td>
<td></td>
</tr>
<tr>
<td>Divorced (n=38)</td>
<td>18.4 (7)</td>
<td>81.6 (31)</td>
<td>9.5 (38)</td>
<td></td>
</tr>
<tr>
<td>Widowed (n=12)</td>
<td>25.0 (3)</td>
<td>75.0 (9)</td>
<td>3.0 (12)</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (n=119)</td>
<td>27.0 (32)</td>
<td>73.0 (87)</td>
<td>30.0 (119)</td>
<td>12.5 (1)</td>
</tr>
<tr>
<td>No (n=281)</td>
<td>12.5 (35)</td>
<td>87.5 (246)</td>
<td>70.0 (281)</td>
<td></td>
</tr>
</tbody>
</table>

HPV, human papillomavirus; SD, standard deviation.

* p < 0.001.
Table 2
Sexual behavior characteristics of the study cohort

<table>
<thead>
<tr>
<th>HPV-positive (n=67)</th>
<th>HPV-negative (n=377)</th>
<th>Total % (N=400)</th>
<th>Chi-square (df)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at first intercourse, mean (SD)</td>
<td>22.0 (4.89)</td>
<td>21.42 (4.57)</td>
<td>t-value = 0.74</td>
</tr>
<tr>
<td>Lifetime sexual partners</td>
<td></td>
<td></td>
<td>8.8 (2)*</td>
</tr>
<tr>
<td>1 (n=352)</td>
<td>16.0 (56)</td>
<td>84.0 (296)</td>
<td>88.4 (352)</td>
</tr>
<tr>
<td>2 (n=30)</td>
<td>13.3 (4)</td>
<td>86.7 (26)</td>
<td>7.5 (30)</td>
</tr>
<tr>
<td>≥3 (n=16)</td>
<td>44.0 (7)</td>
<td>56.0 (9)</td>
<td>4.0 (16)</td>
</tr>
<tr>
<td>Number of sexual partners, mean (SD)</td>
<td>1.3 (0.76)</td>
<td>1.14 (0.48)</td>
<td>t-value = 1.6</td>
</tr>
<tr>
<td>Number of children, mean (SD)</td>
<td>5.44 (2.48)</td>
<td>4.79 (2.56)</td>
<td>t-value = 1.75</td>
</tr>
<tr>
<td>Contraceptive use</td>
<td></td>
<td>0.38 (1)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contraception type</td>
<td></td>
<td>3.5 (3)</td>
<td></td>
</tr>
<tr>
<td>None used</td>
<td>19.0 (21)</td>
<td>81.0 (92)</td>
<td>28.0 (113)</td>
</tr>
<tr>
<td>Condom</td>
<td>0.0 (0)</td>
<td>100.0 (5)</td>
<td>1.3 (5)</td>
</tr>
<tr>
<td>IUD</td>
<td>14.0 (24)</td>
<td>86.0 (151)</td>
<td>44.0 (175)</td>
</tr>
<tr>
<td>Oral pills</td>
<td>21.0 (22)</td>
<td>79.0 (85)</td>
<td>27.0 (107)</td>
</tr>
<tr>
<td>Contraception use duration in months, mean (SD)</td>
<td>50.41 (50.22)</td>
<td>47.58 (35.57)</td>
<td>t-value = 0.46</td>
</tr>
</tbody>
</table>

HPV, human papillomavirus; SD, standard deviation; IUD, intrauterine device.

* p < 0.01.

4. Discussion

The present study determined the prevalence of genital HPV genotypes among women in a hospital-based cohort in Saudi Arabia, as well as the sociodemographic characteristics and sexual behaviors that may be risk factors for HPV infection, which can lead to cervical cancer. Approximately 17% of the women tested positive for HPV, which is in agreement with studies reporting a higher HPV prevalence in Saudi Arabia, as opposed to those suggesting a very low prevalence. Among those reports claiming a higher prevalence of HPV in Saudi Arabia, one recent study screened 519 cervical specimens using PCR and a reverse line blot hybridization assay and found that 164 (31.6%) women were positive for HPV. The results of a recent observational cross-sectional study investigating the prevalence of HPV in women during their routine gynecological examinations at three hospitals in Saudi Arabia, detected HPV DNA in 9.8% of the women (n = 417, aged >15 years). The HPV test was conducted using PCR, and typing was performed using the SPF10 DEIA/LiPA25 system. The discrepancy among the reported results may be attributable to the different detection techniques used in the studies. It was noticed that most studies reporting high rates of HPV used amplification techniques (e.g., PCR and nested PCR), whereas many studies reporting a low prevalence used hybridization techniques (e.g., in situ hybridization and HC-2). Hybridization techniques are known to have lower detection limits because they detect the exact amount of DNA present in the specimen. By contrast, the amplification techniques amplify a minute amount of DNA to millions of copies for detection. An additional plausible explanation is that the rate of HPV-positive women may be expected to be lower in the target group, which was composed of women attending primary care clinics who had no current gynecological problems, whereas the rate of HPV-positive women may be expected to be higher in referral cases or in women presenting in the clinic with gynecological problems such as bleeding, pain in the lower belly or pelvic, etc.

The most commonly detected HPV types in the present study were HPV-18 (34%) and HPV-16 (19%), followed by HPV-11 (13%), HPV-31 (6%), HPV-58 (4%), HPV-56 (3%), and HPV-42 (3%). These results are in agreement with those from two recent observational cross-sectional studies conducted in Saudi Arabia showing that the most prevalent HPV types included HPV-68/73, HPV-18, HPV-16, HPV-6, HPV-42, HPV-53, HPV-54, and HPV-45. Multiple infections were also detected in the present study in 11% of the HPV-positive samples and were highest in the youngest age group (20–29 years). A number of studies have associated multiple HPV infections with a heightened risk for the development or progression of cervical dysplasia and carcinoma; therefore, follow-up for patients diagnosed with multiple infections is essential.

The HPV genotype prevalence stratified by age indicated that that types of HPV most prevalent in women younger than 40 years old differed from those in women aged over 40 years, and that prevalence declined significantly in women aged >50 years. This finding is in agreement with a number of previous reports and is thought to be correlated with several factors, including a reduced number of sexual partners in older women, as well as slowly developing host immunity and viral clearance. A worldwide meta-analysis of age-specific HPV prevalence revealed that women younger than 34 years have a higher rate of HPV infection than those aged 35 years and older. Furthermore, the HPV prevalence below age 25 or 35 years is higher in less developed than in more developed countries. But overall, there is a trend of continuous decline with increasing age.

The results of this study also revealed that smoking is a very strong predictor of HPV infection (p < 0.001). Although it has been reported extensively that smoking is associated with cervical cancer, further studies are required to evaluate smoking as a risk factor for HPV infection. This finding underscores the need to increase awareness of the adverse consequences of smoking among women. Unfortunately, smoking status (yes/no) was tested, but not smoking duration, frequency, or type or number of cigarettes consumed. Therefore, a larger-scale follow-up study will be conducted to investigate smoking status as a predicator factor for HPV infection.

The relationship between sexual behavior and the prevalence of HPV infection was evaluated in women attending KFSHRC clinics. Compared with women who had one partner (16%), HPV positivity was higher in women with three or more lifetime sexual partners (44%). The odds ratio increased with an increasing number of lifetime sexual partners. It is well known that having multiple sexual partners is a risk factor for HPV infection.

The association of contraceptive use and HPV infection varied slightly among the methods employed. For example, 21% of the participants using oral contraceptive pills tested positive for HPV and 14% of IUD users tested positive. However, 19% of the women using no contraception also tested positive for HPV. It was previously suggested that the use of oral contraceptive pills may be a risk factor for cervical intraepithelial neoplasia because oral contraceptives may lead to DNA damage or alter the susceptibility of cells to oncogenic viruses or chemical carcinogens. Interestingly, in the present study, 100% of the few women who used condoms were protected against HPV infection. Unlike Western societies, condom use is low in the Saudi population. The results of this study indicate that condom use in Saudi Arabia...
should be strongly encouraged as a preventative measure against sexually transmitted infections.

The small sample size of positive HPV cases (n = 67) presented a limitation to the analyses of the data collected, restricting the available analytical approaches and occasionally resulting in wide 95% CI ranges and less precision. Additionally, all women who agreed to participate in this study completed the entire survey. The exclusion of partially completed surveys might have introduced a selection bias. Another limitation is that the women receiving care at KFSHRC usually have higher incomes and higher education levels than the population in general. Nevertheless, this study is one of the first to address HPV infection among women in a conservative society in which merely collecting sexual behavior information and cervical specimens remains challenging. Thus, the present findings on HPV prevalence and sociodemographic and sexual behavior risk factors are valuable.

In conclusion, there is a dearth of studies examining HPV prevalence and sociodemographic characteristics in Saudi Arabia. This report is among the few providing sociodemographic and sexual behavior data from Saudi Arabia. Such valuable information may pave the way for understanding HPV infection in a conservative society, which will lead to a better understanding of the infection in general and, therefore, to its prevention. Future research from this group will include a national study with extensive sociodemographic and sexual behavior data covering all 13 provinces of Saudi Arabia. This is to establish a strong database that can be used to measure the HPV prevalence and the need for awareness and vaccination programs.

Acknowledgements

We are grateful to the nursing staff Maha Aljuaithen and Laila Elbassioni, who helped in the sample collection. We would like to thank Dalia Obaid for her assistance in the statistical analysis. We are also grateful to King Saud University Intern students (Lulwah N. Alsalih, Reham A. Aljuamaa, Raneem S. Alnowaiser, Razan A. Alrows) who contributed to this project. We are thankful to the staff at the Sequencing Core Facility and the Research Center Administration at KFSHRC for their assistance. We thank Hanan Shaarawi and Maureene Delos Reyes for their secretarial and administrative support.

Funding: This study was supported in part by a grant from King Abdulaziz City for Science and Technology (13-MED2127-20).

Conflict of interest: None.

Contributions: FA is the project PI and wrote the manuscript. HK conducted the molecular assays. SM performed the statistical analyses. AT performed the pathology tests. TA, IA, MT, AA, AH, and MA provided the patient samples and participated in the interpretation of the clinical results. MA developed the study design, interpreted the results, and reviewed the manuscript. All authors read and approved the final version of the manuscript before submission.

Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.ijid.2016.04.004.

References