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ORIGINAL ARTICLE

Exploring the relationship between oral high-risk HPV infection and sexual behavior among over 400 medical professionals in Japan

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Abstract

Objectives This study investigated the relationship between oral high-risk HPV (HR HPV) infection and sexual behavior in Japanese medical professionals.

Materials and methods We collected oral specimens and a self–administered questionnaire from 234 men and 171 women.

Results The oral HR HPV infection prevalence was 4.7% (95% confidence interval [CI]: 3.0–7.2]) overall, 7.3% (95% CI: 4.6–11.3) for men, and 1.2% (95% CI: 0.3–4.2) for women. The number of sex partners had a significant influence on this prevalence, with variation by type of sexual behavior. The prevalence of oral HR HPV infection was significantly higher ($p < 0.0001$) among those with more than 20 lifetime overall sex partners (23.8%, 95% CI: 13.5–38.5) or oral sex partners (25.0%, 95% CI: 14.2–40.2). In terms of the number of vaginal sex partners, the prevalence was approximately the same for those with 6–10 (8.3%, 95% CI: 3.9–17.0), 11–20 (11.1%, 95% CI: 5.2–22.2), or more than 20 (11.5%, 95% CI: 4.0–29.0) partners ($p = 0.0043$). Furthermore, dividing the number of vaginal and oral sex partners into four categories (both>5, only vaginal>5, only oral>5, and both≤5), the infection prevalence was significantly higher when both vaginal and oral sex partners were more than five (12.5%, 95% CI: 7.7–19.6). The prevalence was also higher for those who had more oral than vaginal partners, compared with other groups (13.5%, 95% CI: 6.7–25.3).

Conclusions and clinical relevance Oral HR HPV infection in Japan seems to be influenced by sexual behavior, and preventive health efforts such as vaccination and health education should be implemented.

Keywords Oral high-risk HPV · Human papillomavirus · Oral infection · Prevalence · Sexual behavior

Introduction

High-risk human papillomavirus (HR HPV) infection has been found to cause cervical cancer and oropharyngeal cancer, especially of the faucial tonsil and the root of the tongue. The relationship between utero-cervical HR HPV infection and cervical cancer has been studied worldwide since the 1980s (Durst et al. 1983). Furthermore, epidemiologic studies have investigated topics such as HPV infection, colonization, and the ratio of patients with HPV who develop cancer (Ho et al. 1998). The relationship between HPV infection and oropharyngeal cancer was identified at almost the same time as the relationship between HPV infection and cervical cancer; however, fewer epidemiologic studies have been conducted on the relationship between HPV infection and oropharyngeal cancer (Farsi et al. 2015). The rate of oral HPV infection found in previous studies ranges from 0.6% to 35.9% (Antonsson et al. 2014; Cook et al. 2014; D'Souza et al. 2014; Gillison et al. 2012; Tam et al. 2018), but the rate of infection in Japan as a whole, including in urban areas, is unknown. The only available report on this is for the small island of Miyakojima, where

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the rate of oral HPV infection was estimated at 0.1% (Kurose et al. 2004).

Factors affecting oral HPV infection have been examined in other countries, especially the United States. Previous work has found a significant relationship between oral HPV infection and sexual behavior. The specific factors identified include age of sexual debut (Jessica A. Kahn et al. 2002), number of lifetime sexual partners (Antonsson et al. 2014; Cook et al. 2014; D'Souza et al. 2014; Dalla Torre et al. 2016; Gillison et al. 2012), and number of sexual partners in the past year (Antonsson et al. 2014; Cook et al. 2014; Gillison et al. 2012). In Japan, there are a few studies (Japan Family Planning Association 2017) focusing on sexual behavior but no classification between vaginal sex and oral sex. Moreover, no studies have investigated the relationships between these aspects of sexual behavior and oral HPV infection. Additionally, in the Japanese context, there seems to be a tendency for people to find it difficult to talk freely and comfortably about sexual issues. Therefore, it may generally be challenging to conduct studies of sexual behavior targeting the general population because of the possibility that people will resist answering questions about their sexual behavior or fail to reply accurately to these questions.

The HPV vaccination has been recommended worldwide because of the likelihood of developing cancer after HPV infection. The number of HPV types protected against by vaccination has gradually increased to nine strains (WHO 2017), and the inoculation subject was expanded to include boys, in addition to girls, in Australia in 2013 (Australian Government 2017). However, although HPV vaccination with public adjuvant in Japan began in April 2013, the active recommendation of inoculation was suspended in June 2013 because of reports of side reactions of the vaccination, despite several World Health Organization recommendations.

It is important to identify the influential factors and implications of HPV infection in Japan, because there is not enough knowledge regarding the current status of HR HPV infection or the associations between HPV infection and influential factors identified in other countries and there are insufficient measures being taken to prevent HPV infection. We have examined 437 Japanese medical professionals and found that the prevalence of oral HR HPV infection was 4.4% (Cho et al. 2020). Therefore, we designed the present study to investigate the relationship between the oral HR HPV infection and sexual behavior in the same cohort. Medical professionals, were targeted because they were able to understand the importance of this research topic.

Materials and methods

Data collection

The data used in this study were saliva specimens, and self-reported demographic characteristics and sexual behavior. The participants gargled with 10 ml of saline for 30 s after the pharynx was washed using a water jet instrument, and the salvia was collected. The water jet instrument was developed jointly by the University of Osaka and the J. Morita Corporation (Kyoto, Japan). The DNA of the specimens was amplified using PCR–rSSO (GENOSEARCH), and the type of HPV (HR HPV or low-risk HPV) was identified. The procedures for detecting oral HPV infection was detailed elsewhere (Cho et al. 2020).

The content of the self-administered questionnaire was selected carefully with consideration for the sensitivity of sexual issues in Japan. Questions asked about sex, age, smoking history, vaccination, lifetime and past-year number of overall sexual partners (any type of sex), and vaginal and oral sexual behavior. Collected specimens and completed questionnaires were assigned the same ID without connecting the information to specific individuals. From January 2016 to January 2017, we announced to the target participants: medical doctors, nurses, and midwives in three hospitals agreeing to participate in the study.

A total of 437 people (244 men and 173 women) agreed to take part in the specimen collection and to complete the questionnaire. The study began after obtaining ethics approval from the institution of one of the authors. The data collection began after obtaining ethics approval from each participating hospital, as needed. Informed consent was obtained from all individual participants included in this study.

Data analysis

Descriptive statistics were calculated for the collected data. The statistical significance of relationships with oral HR HPV infection was assessed using *t*–tests, Welch's *t* test, X^2 tests, or Fisher's exact test. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using logistic regression models. Sexual behavior was examined in detail because of the above mentioned previous findings indicating that the number of sexual partners and oral sexual behavior affect oral HR HPV. We investigated the relationship between factors with significant differences in HR HPV infection and identified the independent factors based on the Kendall's coefficient of concordance and the Cutoff of the number of partners in overall, vaginal and oral sexual behavior. We analyzed the data using SPSS version 22 and JMP Pro 13 and 14. Two-sided *p* values less than 0.05 were considered statistically significant.

Results

The total number of study participants was 437 (244 men and 193 women). Of these, 405 (234 men and 171 women) were included in the analysis, excluding two people whose HPV

viral infection status could not be determined, six with low-risk HPV infection, 23 with no sexual experience because of no infection of HR HPV, and one with contradictory answers on the questionnaire. The median age was 33 years.

Table 1 summarizes the oral High-risk HPV infection status by demographic data and sexual behavior.

Relationships between HR HPV infection and various factors

The prevalence of oral HR HPV infection was 4.7% overall (95% CI: 3.0–7.2, $n = 19$), 7.3% for men (95% CI: 4.6–11.3, $n = 17$), and 1.2% for women (95% CI: 0.3–4.2, $n = 2$). Compared with women, men had a significantly higher portion of infection ($p = 0.0018$). In terms of age category, there were no infected people aged 50 years or older. The highest infection portions were among those aged 45–49 years (9.4%, 95% CI: 3.2–24.2, $n = 3$) and 35–39 years (7.9%, 95% CI: 3.9–15.4, $n = 7$), although there were no statistically significant differences by age category ($p = 0.3323$). The infection prevalence was 1.9% (95% CI: 0.3–10.1, n = 1) among smokers ($n = 52$) and 5.1% (95% CI: 3.3–7.9, $n = 18$) among nonsmokers ($n = 353$), and the difference was not statistically significant ($p = 0.4891$). Only 22 participants had received the HPV vaccination, and none of these participants were infected with oral HR HPV.

There were significant relationships between oral HR HPV infection and sexual behavior. Age of sexual debut was significantly younger among those with oral HR HPV ($n = 19$, mean = 18.4 ± 1.3 years, 95% CI: 17.8–19.0) than among non–infected people ($n = 386$, mean = 19.7 ± 3.0, 95% CI: 19.4–20.0) ($p = 0.0003$). However, in terms of the duration of sexual activity, there were no significant differences ($p = 0.363$) between those infected with oral HR HPV (mean = 18.2 ± 6.8 years, 95% CI: 14.9–21.5) and non–infected people (mean = 16.5 ± 8.0 years, 95% CI: 15.70–17.31).

The number of partners in each sexual behavior by subgroup analysis

The prevalence of oral HR HPV infection was 7.3% (95% CI: 4.6–11.3, $n = 17$) for men. Assessing factors influencing oral HR HPV infection among the male subgroup, no significant differences were found for age or smoking history. However, there were significant differences by sexual behavior. Compared with uninfected men, men who were infected with oral HR HPV (n = 17) reported a significantly younger age of sexual debut ($p = 0.0051$); this finding was similar to the significant difference by age at sexual debut in the full sample ($p = 0.0003$).

The numbers of lifetime sexual partners overall and oral sex partners were significantly related to oral HR HPV infection among men, but the number of vaginal sex partners was not. The prevalence of oral HR HPV infection was significantly higher for those with more than 20 overall sexual partners (22.2%, 95% CI: 11.7–38.1, $n = 8$) ($p = 0.0118$) and for those with more than 20 oral sex partners (22.2%, 95% CI: 11.7–38.1, n = 8), compared with "5 or less" category ($p = 0.0121$). There were no associations between the portion of HR HPV infection and the number of overall, vaginal, or oral sex partners in the past year.

Concerning the median category of two to five partners and calculating the ORs for the categories of six or more, compared with five or fewer, significant relationships were observed between oral HR HPV infection and men's patterns of the sexual behavior. These significant relationships were similar to those found in the analysis for the total sample (oral HR HPV infection in 14.1% among those with more than five vaginal and oral sex partners vs. 3.7% among those with five or fewer vaginal and oral sex partners, $p = 0.0192$). The OR of having more than five oral and vaginal sex partners for men is reduced by almost half (OR = 4.24, 95% CI: 1.33–13.49), compared with the total sample (OR = 8.14,95 %CI:2.64-25.13) Table 1.

The prevalence of Oral HR HPV for women was 1.2% (95% CI: 0.3–4.2, $n = 2$). Neither age nor smoking history was significantly associated with oral HPV among women, as was the case for the total sample and for the male subgroup. Regarding the lifetime number of partners and the number of partners in the past year, the two infected women both had more than 20 partners, suggesting a relationship between these variables.

Cutoff of the number of partners in overall, vaginal and oral sexual behavior

We divided participants into two groups by the number of overall, vaginal and oral sex partners and figured out which the number of sex partners has more impact on the infection of oral HR HPV. For the number of overall and oral sex partners, significantly higher odds of HR HPV infection were observed for those with over 20 (overall OR = 12.29, 95% CI:4.66_32.44; oral OR = 13.19, 95% CI:4.98_34.94), following in more than 5 (overall OR = 7.07, 95% CI: 2.03_24.66; oral OR = 7.74, 95% CI: 2.52_23.79). On the other hand, for the number of vaginal sex partners, significantly higher odds of HR HPV infection was observed for those with more than 5 (OR = 6.82, 95% CI: 2.22_20.94), following in more than 10 (OR = 3.99, 95% CI: 1.57_10.19) (Appendix).

Vaginal and oral sexual behavioral patterns

There were some significant relationships between oral HR HPV infection and the pattern of sexual behavior in terms of the relative number of vaginal and oral sex partners. We divided the number of vaginal and oral sex partners into four categories (both >5, only vaginal >5, only oral >5, or both ≤5) based on the median category of two to five partners. For

Table 1 Oral high-risk HPV infection status by demogrhaphic data and sexual behavior

		TOTAL					MEN					WOMEN				
		HPV(+) (*n* = 19)	HPV(−) (*n* = 386)	prevalence	95%CI*	*p*-values	HPV(+) (n = 17)	HPV(−) (*n* = 217)	prevalence	95%CI*	p-values	HPV(+) (n = 2)	HPV(−) (*n* = 169)	prevalence	95%CI*	p-values
Age	20–24	1	19	5.26	0.94–24.64	0.3323	0	5			0.745	1	14	7.14	1.27–31.47	0.1311
	25–29	1	67	1.49	0.26–7.98		1	27	3.70	0.66–18.28		0	40			
	30–34	6	140	4.29	1.98–9.03		6	95	6.32	2.93–13.10		0	45			
	35–39	7	89	7.87	3.86–15.36		7	67	10.45	5.15–20.03		0	22			
	40–44	1	31	3.23	0.57–16.19		1	18	5.56	0.99–25.76		0	13			
	45–49	3	32	9.38	3.24–24.22		2	13	15.39	4.33–42.23		1	19	5.26	0.94–24.64	
	Over 50	0	27	0			0	9				0	18			
Smoke	Non-smoke	18	353	5.09	3.25–7.92	0.4891	16	196	8.16	5.09–12.85	0.3207	2	157	1.27	0.35–4.53	1
	Smoke	1	52	1.92	0.34–10.12		1	38	2.63	0.47–13.49		0	14			
HPV Vaccine		0	22				0	1				0	21			
Age of sexual debut	mean (SD)	18.4 (1.3)	19.7 (3.0)			0.0003*	18.5 (1.2)	19.6 (2.7)			0.0051	17 (0)	19.8 (3.3)			<0.0001
The duration of sexual activity	mean (SD)	18.2 (6.8)	16.5 (8.0)			0.363	18 (5.5)	16.6 (7.0)			0.5859	20 (18.4)	16.4 (9.2)			0.4192
No. of lifetime sex partners	1	0	35	na		<0.0001	0	12			0.0118	0	23			0.001
	2_5	3	188	1.60	0.54–4.59		3	88	3.41	1.17–9.55		0	100			
	6_10	4	83	4.81	1.89–11.75		4	50	8.00	3.16–18.84		0	33			
	11_20	2	57	3.50	0.97–11.92		2	48	4.17	1.15–13.98		0	9			
	>=21	10	42	23.81	13.48–38.53		8	36	22.22	11.72–38.08		2	6	33.33	9.68–70.00	
No. of lifetime vaginal sex partners	0	0	8	na		0.0043	0	3			0.1274	0	5			0.0004
	1	8	60	na			0	26				0	34			
	2_5	4	185	2.16	0.84–5.43		4	93	4.30	1.69–10.54		0	92			
	6_10	6	72	8.33	3.88–17.01		6	45	13.33	6.26–26.18		0	27			
	11_20	6	54	11.11	5.19–22.19		6	45	13.33	6.26–26.18		0	9			
	>=21	3	26	11.53	4.00–28.98		1	22	4.55	0.81–21.80		2	4	50.00	15.00–85.00	
No. of lifetime oral partners	0	1	42	2.38	0.42–12.32	p < 0.0001	1	22	4.55	0.81–21.80	0.0121	0	20			0.0004
	1	0	57	na			0	26				0	31			
	2_5	3	165	1.82	0.62–5.21		3	79	3.80	1.30–10.58		0	86			
	6_10	4	66	6.06	2.38–14.57		4	42	9.52	3.77–22.07		0	24			
	11_20	1	35	2.86	0.51–14.53		1	29	3.45	0.61–17.18		0	6			
	>=21	10	40	25.00	14.19–40.19		8	36	22.22	11.72–38.08		2	4	50.00	15.00–85.00	
No. of sex partner in the last year	0	1	57	1.75	0.31–9.29	0.227	1	18	5.56	0.99–25.76	1	0	39			0.026
	1	10	243	4.12	2.25–7.41		10	139	7.19	4.00–12.73		0	104			
	>=2	8	105	7.62	3.91–14.32		6	77	7.79	3.62–15.98		2	28	7.14	1.98–22.65	
No. of vaginal sex partner in the last year	0	1	75	1.33	0.24–7.17	0.1058	1	28	3.57	0.63–17.71	0.7644	0	47			0.0224
	1	10	233	4.29	2.35–7.72		10	135	7.41	4.07–13.10		0	98			
	>=2	8	97	8.24	4.24–15.44		6	71	8.45	3.93–17.24		2	26	7.69	2.14–24.14	
No. of oral sex partner in the last year	0	5	126	3.97	1.71–8.95	0.09	5	60	8.33	3.61–18.07	0.5182	0	66			0.019
	1	6	192	3.13	1.44–6.65		6	111	5.41	2.50–11.29		0	81			
	>=2	8	87	9.20	4.73–17.11		6	63	9.52	4.44–19.26		2	24	8.33	2.32–25.85	

Table 1 (continued)

		TOTAL					MEN					WOMEN				
		HPV(+) ($n = 19$)	HPV(−) ($n = 386$)	prevalence	95%CI*	*p*-values	HPV(+) (n = 17)	HPV(−) ($n = 217$)	prevalence	95%CI*	p-values	HPV(+) (n = 2)	HPV(−) ($n = 169$)	prevalence	95%CI*	p-values
Pattern by no. of V&O	Both less than 5	4	232	1.72	0.67–4.34	0.0002	4	107	3.73	1.46–9.22	0.0192	0	125			0.0712
	V > 5&O <=5	0	32				0	20				0	12			
	V <=5&O > 5	0	21				0	15				0	6			
	Both more than 5	15	120	12.50	7.72–19.60		13	92	14.13	8.45–22.69		2	28	7.14	1.98–22.65	
Pattern by the compari-son of V&O	Vaginal = Oral	10	251	3.98	2.18–7.18	0.0109	8	142	5.63	2.88–10.72	0.0181	2	109	1.84	0.50–6.44	1
	Vaginal >Oral	2	102	1.96	0.54–6.87		2	56	3.57	0.98–12.12		0	46			
	Vaginal<Oral	7	52	13.46	6.68–25.27		7	36	19.44	9.75–35.03		0	16			

*CI:Confidence interval

participants with more than five vaginal and oral sex partners, the prevalence of infection was significantly higher (12.5%, 95 %CI: 7.72-19.60 vs. 1.7%, 95%CI; 0.67-4.34, $p = 0.0002$; OR = 8.14, 95% CI: 2.88–29.10).

In addition, we assigned participants to one of three groups by the relative number of vaginal and oral sex partners (vaginal sex partners > oral sex partners, vaginal sex partners < oral sex partners, or vaginal sex partners = oral sex partners) and assessed the portion of oral HR HPV infection in each group. The prevalence of infection was significantly higher for those with more oral sex partners than vaginal sex partners (13.5%, 95%CI: 6.68-25.27), compared with those with equivalent numbers of both types of partners (4.0%, 95%CI: 2.18-7.18) and those with fewer oral sex partners than vaginal sex partners (2.0%, 95%CI: 0.54-6.87, $p = 0.0109$).

Multivariate regression analysis

There are more significant differences of Odds ratios in the multivariate regression analysis among the factors with significant differences in univariate regression. The odds ratios are significantly higher in Smoke (OR = 8.33, 95%CI:1.02–68.88), the pattern of vaginal and oral sex partners (both>5) (OR = 8.87, 95%CI: 2.69–29.22) and the relate number of vaginal and oral sex partners (vaginal sex partners < oral sex partners) (OR = 3.90, 95%CI: 1.26–12.00) (Table 2). Furthermore, putting into the higher number of sex partners (>20), the odds ratios are still significantly higher in smoke, the pattern of vaginal and oral sex partners (both>5) but not in the relationship between the relate number of oral vaginal and oral sex partners. The lifetime sex partner (>20) is significantly higher (OR = 7.14, 95%CI:1.62–31.53/ OR = 31.8, 95%CI: 3.45–293.80) but significantly lower in the number of vaginal sex partners (>20) (OR = 0.04, 95%CI: 0.002–0.54).

Discussion

This study aimed to increase understanding of oral HR HPV infection in urban areas, to elucidate the relationship between oral HR HPV infection and sexual behavior, and to clarify the current situation regarding HR HPV infection and specific sexual behavior for the first time in Japan.

Demographic data

The overall prevalence of oral HR HPV found in this study was 4.7%, which was more than the previous finding of 0.6% for all kinds of HPV in a regional area in Japan (Kurose et al. 2004). The present study identified several characteristics for oral HR HPV infection in Japan that were similar to the findings of previous studies. The oral HR HPV infection prevalence was significantly higher among men than among women in this study

Table 2 Univariate and multivariate regression analysis among factors with significant differences of oral high-risk HPV infection

	HPV(+) (n = 19)	HPV(−) (n = 386)	Univariate Crude OR (95%CI*)	Multivariate Adjusted OR (95%CI*)	Multivariate Adjusted OR (95%CI*)	Multivariate Adjusted OR (95%CI*)
Sex						
Female, n	2	169	Ref.	Ref.	Ref.	Ref.
Male, n	17	217	6.62 (1.51–29.05)	3.99 (0.84–18.84)	4.21 (0.84–21.11)	4.22 (0.83–21.49)
Non-smoke, n	1	51	Ref.	Ref.	Ref.	Ref.
Smoke, n	18	335	2.74 (0.36–20.97)	8.33 (1.02–68.88)	9.63 (1.02–90.46)	12.77 (1.23–132.83)
Age of sexual debut						
<18	5	74	Ref.	Ref.	Ref.	Ref.
> = 18	14	312	1.51 (0.53–4.31)	0.88 (0.27–2.84)	0.70 (0.21–2.34)	0.70 (0.21–2.41)
No. of lifetime sex partners						
<21	9	354	Ref.		Ref.	Ref.
> = 21	10	32	12.29 (4.66–32.44)		7.14 (1.62–31.53)	31.8 (3.45–293.80)
No. of lifetime vaginal sex partners						
<11	10	315	Ref.		Ref.	
> = 11	9	71	3.99 (1.57–10.19)		0.23 (0.05–1.19)	
<21	16	363	Ref.			Ref.
> = 21	3	23	2.96 (0.80–10.89)			0.04 (0.002–0.54)
Pattern by no. of vaginal and oral sex partners						
Either less than 5	4	281	Ref.	Ref.	Ref.	Ref.
Both more than5	15	105	10.04 (3.26–30.93)	8.87 (2.69–29.22)	10.38 (2.39–41.15)	6.32 (1.74–22.92)
Pattern by relative no. of vaginal and oral sex partners						
vaginal = oral	10	241	Ref.	Ref.	Ref.	Ref.
vaginal > oral	2	100	0.48 (0.10–2.24)	0.76 (0.15–3.79)	1.14 (0.21–6.26)	0.51 (0.09–2.96)
vaginal < oral	7	45	3.75 (1.36–10.36)	3.90 (1.26–12.00)	2.84 (0.81–10.02)	0.51 (0.05–4.75)

*CI:Confidence interval

(Antonsson et al. 2014; D'Souza et al. 2014; Gillison et al. 2012). However, age (Gillison et al. 2012) and smoking history (Cook et al. 2014; Gillison et al. 2012; Kreimer et al. 2013), which previous studies identified as influential factors for HPV infection, were not found to be significant in the present study focusing on HR HPV. Previous studies found that 22.6%–42.0% of the population were smokers (Cook et al. 2014; Dalla Torre et al. 2015; Gillison et al. 2012; Kreimer et al. 2013; Tam et al. 2018), and a previous study in Japan found that 30.2% of men and 8.2% of women aged over 20 were regular smokers (Ministry of Health 2016). In contrast, this study found smoking rates that were reduced by almost half, compared with those found in previous work: 12.8% overall, 16.2% for men, and for women 8.2%. There may have been fewer smokers because our study participants were health care providers. The present study did not find a significant relationship between smoking status and HPV infection, although the smokers is significantly higher odds in multivariate regression.

Sexual behavior

In line with the results of studies in other countries, the present study found that oral HR HPV infection in Japan was affected by sexual behavior. There were no significant differences in oral HR HPV infection by duration after the initiation of sexual behavior, but the age of sexual debut was younger among participants with oral HR HPV infection. The association between oral HR HPV infection and age of sexual debut was similar to that found in previous studies (Jessica A. Kahn et al. 2002). The mean age of sexual debut among those infected with HR HPV in this study was 19 years, which was approximately the same age as has been reported in previous Japanese studies (Japan Family Planning Association 2017). This was about two years older than Kahn et al.'s (2002) finding of 16.7 years and D'Souza's (D'Souza et al. 2014) results, 17.0 year old. Together, these findings indicate that Japanese sexual debut occurs in the late teens, which may be relatively late, compared with findings for other countries.

Furthermore, the number of lifetime sexual partners affects oral HPV infection (Antonsson et al. 2014; Cook et al. 2014; D'Souza et al. 2014; Dalla Torre et al. 2016; Gillison et al. 2012; Kero et al. 2014). D'Souza et al. (2014) found a significant relationship between HPV infection and having five and more of both vaginal and oral sex partners, and Dalla Torre et al. (2015) reported associations between oral HR HPV infection and having more than 10 total vaginal and oral sex

partners. The present study found highly significant relationships between HR HPV infection and having more than five partners and, especially, more than 20 partners.

Observing the pattern of the number of vaginal and oral sex partners, the effect of oral sex seems to be significantly more important for predicting oral HR HPV infection, especially if the number of oral sex partners is higher than the number of vaginal sex partners. Most of the participants in this study (62.0%) reported the same number of vaginal and oral sex partners, 25.2% reported more vaginal sex partners, and 12.8% reported more oral sex partners. The infection portion was 35% among the group with more oral sex partners than vaginal sex partners, and this difference was significant. D'Souza et al. (2014) showed that around 60% had more vaginal than oral sex partners, 30% had equal numbers of both types of sex partners, and 10% had more oral than vaginal sex partners. Notably, the present study found that approximately 70% of participants had more oral than vaginal partners or equivalent numbers of both types of partners, which is more than was found in the previous study. In addition, among whites in the United States (who have been found to differ significantly from other racial groups), a previous study found that 20.8% of men and 7.1% of women had more than 10 oral sex partners(D'Souza et al. 2014). However, the present study found that 26.9% of men and 6.1% of women had more than 10 oral sex partners, which may indicate a higher level of oral sex experience among the men in this study than that reported for men in the United States.

In contrast to previous studies, which mainly focused on all kinds of HPV infection, this study focused only on HR HPV infection, finding several characteristics of sexual behavior to be important predictors. However, this study did not assess other factors that previous research in other countries has identified as potentially influential for oral HPV infection, such as marital history (Kero et al. 2014; Kreimer et al. 2013), alcohol use (Cook et al. 2014; Dalla Torre et al. 2016; Jessica A. Kahn et al. 2002), drug use (Antonsson et al. 2014; Cook et al. 2014; Jessica A. Kahn et al. 2002), history of sexually transmitted infections (Antonsson et al. 2014; Jessica A. Kahn et al. 2002), and more detailed sexual behavior (Cook et al. 2014; Gillison et al. 2012).

Implications for health efforts

The present findings regarding the relationships between oral HR HPV infection and sexual behavior have several implications for HPV infection prophylaxis in Japan. First, the findings could lead to further self-care action through better understanding of the current status of HPV infection of the pharynx. In Japan, acting on this knowledge would be useful, because there are not currently enough efforts to prevent HPV infection in this context, where the active recommendation of the HPV inoculation was discontinued in June 2013 because of news reports of the side reactions of the vaccine. The number of patients with cervical cancer has increased in Japan, especially among younger people (FPCR 2017). Furthermore, the cervical cancer screening rate among Japanese women was 42.4% as of 2016 (Comprehensive Survey of Living Conditions), which is approximately 20% lower than the screening rate in other countries (OECD_STAT). Previous work has pointed to the difficulties women face in seeking gynecologic consultation as one of the reasons for not attending cervical cancer screenings in Japan (Shimizu et al. 2013). Although differences in individual conditions should be considered, an overall understanding of the status of oral HR HPV infection in Japan should be useful for men and women. Tam et al. (2018) reported that previous studies found the duration of oral HR HPV (HPV 16) clearance to range from 3.5 months to 20.7 months. Furthermore, several studies (Kero et al. 2014) have identified differences between genital and oral HPV infection in men and women. Kero et al. (2014) investigated spouse's oral and genital HPV infection longitudinally: Among men, cases of oral and genital HPV infection were approximately equal, whereas there were more cases of genital than oral HPV infection among women. In a government-sponsored public health study (Mikamo et al. 2016), the congruity of urinary and the utero-cervical HPV infection was assessed, but there was no conclusions could be drawn on this because of a sensitivity of 68.4% and a specificity of 99.8%. Although this technique might not provide a full assessment of HPV infection status, sampling saliva to determine HPV infection of the pharynx is simple and avoids stresses caused by the sense of shame among participants, particularly in Japan. Considering the cultural characteristics and current situation in Japan, understanding HPV infection of the pharynx in this context may serve as an incentive to undergo consultation for cervical cancer examination.

Second, the study results highlight the necessity of the HPV vaccination to prevent HPV infection and suggest the need to extend inoculation to men as well as women. The prevalence of HPV infection and morbidity from diseases associated with the HPV infection are significantly lower for the generation of people who were vaccinated against HPV in other countries (Ali et al. 2013; Markowitz et al. 2013). A similar tendency has been observed among non-inoculators, possibly because of "herd immunity (Ali et al. 2013; Tabrizi et al. 2014)". Furthermore, similar results have been found among the inoculated generation in Japan (Konno et al. 2018; Yagi et al. 2017), despite of the short term of inoculation among the general population. Concerning the potential of HPV vaccination to promote sexual behavior, research comparing vaccinated and unvaccinated people has found non-significant differences in sexual behavior (Hansen et al. 2014), and a positive relationship between receiving the vaccination and using condoms and other methods of safer sex (Mullins et al. 2016). As mentioned above, sexual behavior,

oral HR HPV infection, and oropharyngeal cancer have been demonstrated to be closely linked, and significantly more men than women are infected with oral HR HPV. This may indicate that HPV inoculation should not be recommended only for women, but also for men.

Finally, based on the relationship between oral HR HPV infection and sexual behavior, it is necessary to improve reproductive health in adolescence and adulthood by sharing appropriate information, including through health education. Examinations of the link between oral HR HPV infection and the development of cancer are ongoing. Farsi et al. (2015) have conducted systematic reviews to investigate the association of head and neck cancer with sexual behavior, finding no direct effect but a few possibilities of sociodemographic and behavioral influences. Contraception, to prevent both sexually transmitted infections and unwanted pregnancy, is currently included in the sex education and life education curricula in Japan. However, the present conditions regarding sexual behavior and contraception are not fully discussed because of an inclination toward "*Netako–wo Okosuna*," which means "do not make children aware of it if they are not already." Previous work has shown that oral HR HPV infection does not differ significantly by contraceptive behavior (Gillison et al. 2012), although it is significantly associated with sexual behavior. Oral HR HPV infection may lead to cervical cancer or pharyngeal cancer in the mid- or long term. Providing education regarding sexual behavior decisions and safer sex may be necessary because of the health impact of the possibility of developing cancer in the long term.

Limitations and future perspectives

The educational background of the participants in the present study may have biased the results, because the participants, as health care professionals, generally had higher levels of education compared with the general population. Therefore, it may be problematic to generalize the findings of this study to the overall Japanese population. However, previous studies have found that educational background is not an influential factor for HPV infection (Gillison et al. 2012). A second limitation is that this study did not examine the relationships between oral HPV infection and martial history, detailed sexual behavior, sharing items such as lipstick or a toothbrush, and contraceptive use; this is a limitation because these factors have sometimes been identified as influential in previous research.

Another study limitation is that we could not analyze the numbers of different types of sexual partners more precisely, instead adopting categories for these variables to allow the participants to answer more easily. Further research that takes into account the sensitivity of sexual issues in Japan is needed to investigate the relationship between the oral HR HPV infection and several additional factors identified in previous research. Clarifying detailed suggestions for further health efforts is also a challenge that should be taken up by future work.

Conclusions

The prevalence of oral HR HPV infection was 4.7%, and this portion was significantly higher among men than among women. Oral HR HPV infection seems to be influenced by smoke, the number of sexual partners and by the pattern of vaginal and oral sex partners. There may be more impact on oral HR HPV infection when the number of overall and oral sex partners is more than 20, when the numbers of both oral and vaginal sex partners are more than five, and when the number of oral sex partners is larger than the number of vaginal sex partners. Considering these associations and Japanese perspectives of sexual issues, we suggest assessing HPV infection status using saliva samples, and we stress HPV vaccination and education on the relationship between HPV infection and sexual behavior as potentially beneficial health efforts.

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Compliance with ethical standards

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