ORIGINAL ARTICLE

Bali Medical Journal (*Bali Med J)* 2020, Volume 9, Number 3: 646-653
P-ISSN.2089-1180, E-ISSN: 2302-2914

Published by DiscoverSys

Prevalence of and risk factors associated with anal HPV infection among men who have sex with men in Bali, Indonesia

I Ketut Agus Somia[1*], Tuti Parwati Merati[1], Dewi Dian Sukmawati[1], I Gusti Ayu Agung Elis Indira[2], Ida Bagus Nyoman Putra Dwija[3], Made Yogi Oktavian Prasetia[4], Nittaya Phanuphak[5], Siriporn Nonenoy[5]

ABSTRACT

Background: Anal human papillomavirus (HPV) is one of the most common sexually transmitted infection. Men who have sex with men (MSM) are commonly affected by anal HPV infection. Until now, there is no data available on the prevalence of HPV genotype in the MSM in Indonesia

Purpose: This study aimed to determine the prevalence and risk factors of anal HPV infection among MSM in Bali, Indonesia.

Patients and methods: A cross-sectional study was conducted among MSM in Sanglah Hospital, Bali, Indonesia. Blood samples were collected for HIV serological testing and syphilis serological screening, and anal swabs were collected for HPV genotyping. Risk factors associated with anal HPV infection were assessed by univariate and multivariate logistic regression. Anal HPV infections were also being categorized into any anal HPV types, HR HPV types, LR HPV types, and multiple HPV types.

Results: Mean age of participants was 31.4 years. The prevalence of HPV infection was 89.3% and 61.3% for coinfection between LR and HR types. Almost half of our participants had at least two HR anal HPV and they were co-infected with HPV 16, 39, and 51. Participants with HIV infection were associated with anal HPV, LR HPV, and multiple HPV types of infections.

Conclusion: HIV status were associated with anal HPV infection among MSM in Bali, Indonesia. Since all of the participants with at least two anal HPV genotypes were co-infected with HPV 16, 39, and 51, it is to be hoped that HPV vaccination can be introduced into MSM communities in Bali, Indonesia.

Keywords: Papillomavirus infection; men who have sex with men; HIV infections

Cite this Article: Somia, I.K.A., Merati, T.P., Sukmawati, D.D., Indira, I.G.A.A.E., Dwija, I.B.N.P., Prasetia, D.D., Phanuphak, N., Nonenoy, S. 2020. Prevalence of and risk factors associated with anal HPV infection among men who have sex with men in Bali, Indonesia. *Bali Medical Journal* 9(3): 646-653. DOI: 10.15562/bmj.v9i3.2087

[1]Tropical and Infectious Disease Division, Department of Internal Medicine, Universitas Udayana-Sanglah Hospital, Bali, Indonesia
[2]Department of Dermatology and Venerology, Universitas Udayana - Sanglah Hospital, Bali, Indonesia
[3]Clinical Microbiology Universitas Udayana - Sanglah Hospital, Bali, Indonesia
[4]Nusa Indah VCT Clinic, Sanglah Hospital, Bali, Indo,nesia
[5]Prevention Department, The Thai Red Cross AIDS Research Centre, Bangkok Thailand

*Corresponding to:
I Ketut Agus Somia;
Tropical and Infectious Disease Division, Department of Internal Medicine, Universitas Udayana-Sanglah Hospital, Bali, Indonesia;
agus.somia@unud.ac.id

Received: 2020-09-18
Accepted: 2020-11-05
Published: 2020-11-25

INTRODUCTION

Anal human papillomavirus (HPV) is one of the most common sexually transmitted infections, causing a substantial burden of disease in men and women.[1-3] Men who have sex with men (MSM) are commonly affected by anal HPV infection. Human immunodeficiency virus (HIV)-infected MSM are at exceptionally high risk of anal HPV infection and infection with multiple genotypes.[1-6] Other risk factors associated with HPV infection are smoking and sexual practices.[7]

Until now there is no data available on the prevalence and distribution of HPV genotype in the MSM in Bali province and Indonesia.[8] Therefore, this study aimed to assess the prevalence of and associated risk factors for anal HPV infection among MSM in Bali, Indonesia.

MATERIAL AND METHODS

Study design

This study was a cross sectional study at Nusa Indah Clinic Sanglah Hospital, an HIV and sexual transmitted diseases referral center in Bali, Indonesia. Participants were recruited from 22nd June 2011 to 13th February 2012. by asking participants to pass on our contact details to their friends (snowballing sampling). Basic demographic data, along with information regarding sexual behavior, were collected by means of a self-completed questionnaire.

Informed consent and ethics

The study was approved by the institutional review board of Kerti Praja Foundation with ethical clearance No 027/IRB-YKP/2011 and was supported by NIH (National Institute of Health) / President's emergency fund for AIDS Relief (PEPFAR).

Data collection

Eligibility criteria were as follows: (1) Men aged 18 years or older, (2) has a history of anal sexual intercourse with men, (3) willing to provide blood samples for HIV and syphilis serologies

and anal swab specimens to test HPV infection and genotypes, and (4) able and willing to provide written informed consent.

Demographic data (including age, education, and employment status), sexual history (including sexual activity in the last 6 months), smoking status, and alcohol consumption were collected at enrollment. We used 30 years old as a cut-off point for age since the median age is 31 years old. We used senior high school (grade 9) for the cut-off point for education because of the 9-year compulsory education program. Positive smoking status was defined as current smokers and ex-smokers. Positive alcohol consumption was defined as participants who consumed any type of alcohol more than 12 drinks per year.

Laboratory test

Blood samples were collected for HIV serological testing (anti-HIV) and syphilis serological screening (VDRL serology tests and TPHA test). Anti-HIV tests were conducted with 3 different rapid test methods i.e., VIKIA® HIV 1/2 (bioMérieux, France), HIV 1 & 2 Antibody Rapid Test Oncoprobe (Oncoprobe Utama, Indonesia), and HIV InTEC 1/2 rapid test (InTEC, China). HIV-positive status was defined as three reactive rapid tests. VDRL serology tests were performed using syphilis toluidine red untreated serum test (TRUST). TPHA tests were done with rapid serological, immunochromatographic assay for detection of antibodies to syphilis antigen in human serum or plasma. Positive syphilis was defined as a reactive result in VDRL and TPHA test. Those with positive syphilis were treated with penicillin intramuscular unless there is any contraindication.

A trained physician collected anal swab samples for HPV genotyping by rotating a moistened and non-lubricated flocked swab in the anal canal without direct visualization. The collected samples were being stored in the liquid cytology media Thin Prep® PAP test PreservCyt® solution (Hologic Inc, USA). Anal swab specimens were then being stored in -80° C at Molecular Biology Laboratory in the Faculty of Medicine, Universitas Udayana, Bali Indonesia.

HPV genotyping was done using the Linear Array HPV Genotyping Test (Roche Molecular System, USA) at Clinical Pathology Laboratory Dharmais Cancer Hospital, Jakarta, Indonesia. The test amplified target DNA within the polymerase L1 region of HPV genome (450 base pairs) by the polymerase chain reaction (PCR). The test then utilized nucleic acid hybridization to independently identify 37 anogenital HPV DNA genotypes (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 54, 55, 56, 58, 59, 61, 62, 64, 66, 67, 68, 69,70,71,72,73 (MM9), 81, 82 (MM4), 83 (MM7), 84 (MM8), IS39 and CP6108) in cells.

Statistical analysis

HPV prevalence was defined as having a specific HPV genotype at enrolment visit. High risk (HR) HPV types are HPV with genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68.[9] HR HPV types are commonly known as oncogenic HPV.[9] Low risk (LR) HPV types are HPV with genotypes 6, 11, 26, 40, 42, 53, 54, 55, 61, 62, 64, 66, 67, 69, 70, 71, 72, 73, 81, 82, 83, 84, IS39, and CP6108.[9] LR HPV types are commonly known as non-oncogenic HPV.[9] Participants were said to have multiple HPV genotypes infection when they were tested positive for two or more HPV genotypes (HR or LR HPV types).

Frequency distributions and descriptive statistics were used to characterize the study sample. Prevalence for any HPV, HR HPV, LR HPV, and multiple HPV types was calculated. Descriptive statistics were calculated to describe the most prevalent genotypes in each group (any HPV, HR HPV, LR HPV, and multiple HPV types). We also conducted a descriptive analysis of participants infected with two high-risk HPV types.

In the univariate analysis, chi-square analysis or Fisher exact tests were used to evaluate differences in categorical outcome measures. Factors of significance level of less than 0.25 in univariate analysis were adjusted in a multivariate logistic regression model using backward selection method to identify risk factors associated with anal HPV infection in four separate models: 1) any HPV types, 2) HR HPV, 3) LR HPV and 4) multiple HPV types as dependent variables. Values of $p<0.05$ were considered statistically significant in multivariate logistic regression. Data were analyzed using SPSS (version 16.0 for Windows; SPSS Inc., Chicago, IL).

RESULTS

Participants' characteristics

There were 90 MSM who were enrolled; eleven out of 90 subjects did not attend when the specimen collection was performed. (Two people were moved to Java, and nine people were still working when the specimens were collected). Out of 79 specimens, 2 (2.5%) invalid specimen and 2 (2.5%) specimens that were failed to be isolated their DNA (un-isolated DNA specimen), and 75 (95.0%) adequate specimens for data analysis. The demographic characteristics of the participant are shown in Table 1.

As can be seen in Table 1, the study participants are mostly aged more than 30 years old, have

finished their grade 9, have jobs, and drunk alcohol less than 12 drinks per year. Regarding their sexual behaviors, most of them have their anal sexual debut when they are under 18 years old, have protected receptive anal intercourse with less than 10 same-sex partners in the last 6 months. Furthermore, most participants have negative syphilis status and positive HIV status.

Table 1. Characteristics of MSM attending in Bali Indonesia

Characteristic	MSM (n = 75)	
	N	%
Age		
Mean ± SD (years)	31.4 ± 7.7	
Median (years) (IQR)	31 (25-38)	
18 – 30 years	34	45.3
> 30 years	41	54.7
Education		
Lower than senior high school (Grade 9)	26	34.7
Senior high school or higher (Grade 9)	49	65.3
Employment status		
Unemployed	15	20
Employed	60	80
Age at first time anal sexual debut		
Mean ± SD (years)	17.0 ± 4.5	
Median (IQR) years	17 (14-20)	
≤ 18	52	69.3
>18	23	30.7
Number of sex partners in the last 6 months		
Median (IQR)	3 (2-5)	
>10	23	30.7
≤ 10	52	69.3
Condom use in the last 6 months		
No/ sometimes	25	33.3
Always	50	66.7
Receptive anal intercourse in the last 6 months		
Yes	58	77.3
No	17	22.7
Circumcision		
No	37	49.3
Yes	38	50.7
Smoking (Current Smokers and Ex-Smokers)		
Yes	37	49.3
No	38	50.7
Alcohol consumption		
Yes	23	30.7
No	52	69.3
Syphilis		
Yes	16	21.3
No	59	78.7
HIV		
Yes	47	62.7
No	28	37.3

Abbreviations: MSM, men sex with men

Prevalence of any, multiple, HR and LR anal HPV infection

From 75 participants, there were 67 participants (89.3%) found to be infected with any anal HPV infection (Table 2). 54 participants (80.6%) had multiple anal HPV infections (more than 1 HPV genotype), and 46 of them (61.3%) had coinfection between HR and LR anal HPV infection. LR anal HPV genotypes were detected in 52 participants (69.3%). Of these 33 (44.0 %) had multiple LR HPV genotypes. HR anal HPV genotypes was detected in 61 participants (81.3 %) and 33 (44.0%) had multiple HR HPV genotypes (Table 2).

Specific anal HPV

The most common LR anal HPV genotype found (Figure 1) was HPV 62 (18.66%), HPV 6 (17.9%), HPV 11 (14.66 %), followed by HPV 61 (12.0 %), HPV 70 (12.0%). While, HPV 16 (26.7%) was the most common HR anal HPV genotype found among MSM (Figure 2), followed by HPV 51 (25.3%), HPV 52 (22.7%), HPV 18 (21.3%), HPV 58 (13.33%), and HPV 59 (12.0%).

Among 33 participants with multiple anal HR HPV infections, all were co-infected with HPV 16, 39 and 51. The combination of HR anal HPV co-infection, statistically significant were anal HPV 18 and 31 (12.5%), anal HPV 33 and 35 (66.7 %), anal HPV 33 and 59 (66.7%), anal HPV 39 and 51 (71.4%), anal HPV 39 and 58 (42.9%), and anal HPV 58 and 68 (30%) (Table 3)

Factor associated with any anal HPV, multiple anal HPV, HR and LR anal HPV.

We examined potential factors associated with any HR, LR, and multiple anal HPV infections. First, we conducted a univariate analysis for each potential risk factor using Chi-square analysis or Fisher exact tests. In any anal HPV infection group, we found positive alcohol consumption (any type of alcohol more than 12 drinks per year) and positive HIV status as the significant factors ($p<0.25$) to be included in the multivariate analysis (Table 4). In the high risk (HR) anal HPV infection group, lower education (lower than senior high school/grade 9), more than 10 same-sex partners in the last 6 months, and positive HIV status were included in the multivariate analysis. In the low risk (LR) anal HPV infection group, unemployment, receptive anal intercourse in the last 6 months, smokers (current smokers and ex-smokers), positive syphilis, and HIV status were significant factors to be included in the multivariate analysis. In the multiple anal HPV infections, we found a lower education level (lower than grade 9) and positive HIV status as the significant factors to be included

Published by DiscoverSys | *Bali Med J* 2020; 9(3): 646-653 | doi: 10.15562/bmj.v9i3.2087

Table 2. Prevalence and number of anal HPV infection among MSM in Bali, Indonesia

Variable	MSM	
	N = 75	%
HPV DNA positive	**67**	**89.3**
Number of HPV genotypes		
None	8	10.7
Single HPV type	13	17.3
Coinfection between 2 HPV types	12	16.0
Coinfection between 3 HPV types	10	13.3
Coinfection between >3HPV types	32	42.7
Median (IQR)	3 (1-5)	
Low and high-risk HPV infection		
None	8	10.7
Only low risk (LR) HPV infections	6	8.0
Only high risk (HR) HPV infections	15	20.0
Coinfection LR and HR HPV types	46	61.3
Number of HR HPV genotypes		
None	14	18.7
Single HR HPV type	28	37.3
Coinfection between 2 HR HPV types	17	22.7
Coinfection between 3 HR HPV types	12	16.0
Coinfection between >3 HR HPV types	4	5.3
Median (IQR)	1 (1-2)	
Number of LR HPV genotypes		
None	23	30.7
Single LR HPV type	19	25.3
Coinfection between 2 LR HPV types	14	18.7
Coinfection between 3 LR HPV types	6	8.0
Coinfection between >3 LR HPV types	13	17.3
Median (IQR)	1 (0-3)	

Abbreviations: MSM, men sex with men

in the further analysis.

Table 5 showed that the odds ratio (OR) of respondents with positive HIV status in cases who had any anal HPV infection, low risk anal HPV infection, and multiple HPV infection were 12.31 (95% CI: 1.39 to 109.08; p=0.02), 12.90 (95% Cl: 3.00 to 55.10; p<0.01), and 3.71 (95% CI: 1.26 to 10.98; p=0.02). We also found that the odd of exposure of lower education level (lower than grade 9) was 7.02 times higher among cases of LR anal HPV infection than with controls who have higher education level (95% CI: 1.12 to 44.13; p=0.04). Interestingly, negative syphilis infection status was associated with a lower incidence of LR anal HPV infection (OR: 0.19; 95% CI: 0.05 to 0.82, p=0.03)

DISCUSSION

As far as we know, this was the first study on the prevalence and genotype distribution of anal HPV infection among MSM in Bali, Indonesia. We found that 89.30% of respondents had any anal HPV infections in 2011- 2012. The high prevalence of any anal HPV infection among MSM was also mentioned in other developing countries, such as in the northern Thailand (80.00%) in 2012-13; and Nigeria in 2013 (85.06%), Central African (69.1%).[10-12] Furthermore, a meta-analysis study on any anal HPV types in MSM has also revealed that 92.6% (95% CI: 90.8 – 94.5) in HIV patients and 63.9% (95% CI: 55.2-72.6) in non-HIV patients.[13] Like other studies in the developing countries.[10-12] most participants were young adults in their 20s and 30s with adequate education (primary or secondary

Table 3. The number and percentage of coinfection among anal HR HPV genotypes in MSM with two or more HR HPV genotype

HPV	16	18	31	33	35	39	45	51	52	56	58	59	68	N
16	-	15	5	5	5	15	15	25	25	5	15	15	20	20
18	18.8	-	12.5*	6.3	12.5	12.5	0	37.5	0	6.3	6.3	6.3	0	16
31	50	100	-	0	50	50	0	50	0	50	50	0	0	2
33	33.3	33.3	0	-	66.7*	33.3	33.3	33.3	0	0	33.3	66.7*	0	3
35	20	40	20	40*	-	40	20	40	40	20	40	20	0	5
39	42.9	28.6	14.3	14.3	42.9	-	28.6	71.4*	28.6	14.3	42.9*	14.3	14.3	7
45	60	0	0	20	20	40	-	20	20	20	20	20	0	5
51	26.3	31.57	5.3	5.3	10.52	26.31*	5.3	-	31.8	5.3	15.78	21.05	5.3	19
52	29.41	0	0	0	11.76	11.76	5.9	35.29	-	5.9	5.9	23.5	11.76	17
56	20	20	20	0	20	20	20	20	20	-	0	0	20	5
58	15	5	5	5	10	15*	5	15	5	0	-	5	15*	20
59	33.3	33.3	0	22.2*	11.11	11.11	11.11	44.44	44.44	0	11.11	-	0	9
68	57.1	0	0	0	0	14.28	0	14.28	28.57	14.28	42.85*	0	-	7

Note: Each row show that percentage of frequency of co infection with other genotypes identified in the next 13 columns. Last column shows the number of samples each genotype. *p< 0.05 in Chi-square analysis or Fisher exact tests

education level). Besides, most respondents in other developing countries have their first-time anal sexual debut when they were lower than 18 years old.[11] Majority of our participants used condoms in their receptive anal intercourse in the last six months.

Our study has found that most of the participants (81.3%) had HR anal HPV type. High prevalence of HR HPV types was also reported in a meta-analysis by Machalek, Poynten.[12] They also reported that 73.5% (95% CI: 63.9 – 83.0) of HIV patients and 37.2% (95%CI: 27.4-47.0) of participants without HIV infection had anal HR HPV infections.[12] Our study result also in line with other studies that HPV 16 is the most common anal HR HPV found in MSM.[8,13,14] Unlike other studies, such as Machalek, et al.[13] and Daling, et al.[6] found that HPV 18 as the second most common anal HR HPV found. It is very different from Central Africa, where HPV 16 and 18 are genotypes of a minority.[12]

In our study, 69.3% of all participants had anal LR HPV infections. HPV 62 was the most common LR HPV genotype found. This result is different from the research of Daling, et al.[7] and Frisch, et

Table 4. Univariate analysis of demographic characteristics, sexual behaviours, syphilis and HIV as factors associated for anal HPV infection

Variables	Any HPV type			Multiple HPV			HR HPV			LR HPV		
	Positive (N:67)	Negative (N: 8)	P	Positive (N:54)	Negative (N:21)	P	Positive (N:61)	Negative (N:14)	P	Positive (N:52)	Negative (N:23)	P
Age (years)												
≤ 30	31	3	0,72	24	10	1.00	29	5	0,56	23	11	0,81
> 30	36	5		30	11		32	9		29	12	
Education												
Lower than high school	25	1	0,29	22	4	0,11	25	1	0,03	19	7	0,79
High school or higher	42	7		32	17		36	13		33	16	
Working												
No	15	0	0,35	12	3	0,54	14	1	0,27	13	2	0,13
Yes	52	8		42	18		47	13		39	21	
Age at first time homosexual behaviour (years)												
≤18	46	6	1.00	37	15	1.00	43	9	0,75	36	16	1.00
>18	21	2		17	6		18	5		16	7	
Number of homosexual partner in the last 6 months												
>10	22	1	0,42	18	5	0,58	21	2	0,20	16	7	1.00
≤ 10	45	7		36	16		40	12		36	16	
Condom use in the last 6 months												
No	24	1	0,26	19	6	0,79	22	3	0,36	18	7	0,80
Always	43	7		35	15		39	11		34	16	
Anal receptive intercourse in the last 6 months												
Yes	51	7	0,65	41	17	0,77	47	11	1.00	38	20	0,24
No	16	1		13	4		14	3		14	3	
Circumcision												
No	32	5	0,48	27	10	1.00	29	8	0,57	26	11	1.00
Yes	35	3		27	11		32	6		26	12	
Smoking												
Yes	32	5	0,48	26	11	0,80	30	7	1.00	23	14	0,22
No	35	3		28	10		21	7		29	9	
Alcohol												
Yes	19	4	0,24	16	7	0,79	18	5	0,75	14	9	0,42
No	48	4		38	14		43	9		38	14	
Syphilis												
Yes	14	2	0,68	11	5	0,76	12	4	0,48	9	7	0,23
No	53	6		43	16		49	10		43	16	
HIV												
Yes	46	1	0,003*	39	8	0,008*	41	6	0,13	38	9	0,009*
No	21	7		15	13		20	8		14	14	

Note: **p< 0.05 in Chi-square analysis or Fisher exact tests*
Abbreviation: HPV, human papilloma virus; HR, high risk; LR, low risk

al.[15] who found the most HPV 6. Whereas in this study HPV 6 was found to be the second-highest (17.9%).

We found that 61.3% of all participants had coinfection between low-risk and high-risk types, and 44% of all participants had at least two anal HR HPV infections. Our data have confirmed previous findings that multiple anal HPV infections are common.[8,16,17] Since anal HR is the primary causal agent of anal cancer, our discussion will focus on the coinfections of two anal HR HPV infections. We found all the HR HPV genotypes were co-infected with anal HPV 16, 39, 51. These three types of anal HR HPV genotypes were also found

Table 5. Factors associated with anal HPV infection among MSM in Bali Indonesia: multivariate logistic regression analyses

Variables	Adjusted Odd Ratio (95% Confidence Interval)			
	Any anal HPV type	HR HPV	LR HPV	Multiple HPV
Education				
Lower than high school		7.19 (0.86-60.12)*		2.30 (0.65-8.17)
High school or higher		Reference		Reference
Employment				
Unemployed			7.02 (1.12-44.13)*	
Employed			Reference	
Number of same sex partners in the last 6 months				
> 10		2.18 (0.41-11.53)		
≤ 10		Reference		
Receptive anal intercourse in the last 6 months				
Yes			0.20 (0.03-1.07)	
No			Reference	
Smoking				
Yes			0.30 (0.80-0.997)	
No			Reference	
Alcohol				
Yes	0.47 (0.09-2.37)			
No	Reference			
Syphilis				
Yes			0.19 (0.05-0.82)*	
No			Reference	
HIV				
Yes	12.31 (1.39 –109.08)*	1.88 (0.54-6.63)	12.90 (3.00-55.10)*	3.71 (1.26-10.98)*
No	Reference	Reference	Reference	Reference

Note: * $p < 0.05$ *in multivariate logistic regression model*

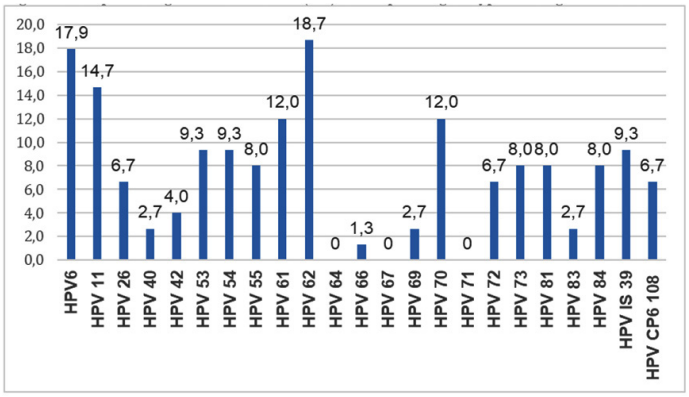

Figure 1. The percentage of anal low-risk (LR) HPV specific genotypes among MSM found

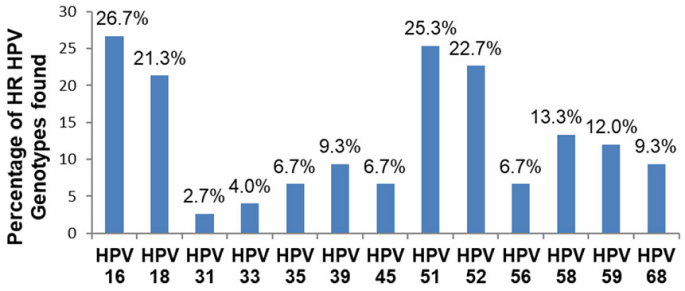

Figure 2. The percentage of high-risk (HR) anal HPV specific genotypes among MSM found

in other studies.[8,18,19] Therefore, it is crucial for the introduction of the HPV vaccine that contains these HR anal HPV genotypes among MSM in Indonesia, especially in Bali.

Our study has revealed that participants with HIV infection were positively associated with any anal HPV (aOR: 12.31, 95%CI: 1.39-109.08), LR HPV (aOR: 12.90, 95%CI: 3.00-55.10), and multiple HPV types infections (aOR: 3.71, 95%CI: 1.26-10.98). Positive HIV status as a significant risk factor is similar to what had been found in Thailand, Nigeria Netherland, and China, where the prevalence of any anal HPV infections was higher in HIV-positive MSM than HIV-negative MSM.[9,11,20,21]

Other than positive HIV status, we also found that positive syphilis status and unemployment as significant factors have an association with LR anal HPV infections. Even though participants without employment had a higher risk of getting LR anal HPV infections, we have not collected other details regarding their jobs. Interestingly, positive syphilis status was inversely associated with LR anal HPV infection. We cannot explain the biological plausibility of this finding.

There are several limitations of this study, as follows. Firstly, our limited number of samples and this hospital-based study may introduce the possibility of sampling bias. We have tried to limit the sampling bias using snowballing sampling and using an HIV and sexual transmitted diseases referral center. The use of snowballing sampling is useful in reaching hard-to-reach populations, such as MSM communities.[22] Secondly, we did not collect more specific information on employment since employment as sex workers is an important risk factor that can clarify these results. Thirdly, we have not found any plausible explanation regarding the possibility of the protective effect of syphilis infection on LR anal HPV infection. Further studies may be needed to explain this association

CONCLUSION

We concluded that the prevalence of anal HPV among MSM in Bali is very high. HIV infection is associated with increased anal HPV infection. Longitudinal research is needed on the incidence, clearance, and persistence of anal HPV and diseases related to HPV in MSM, especially among those with HIV infection, those without jobs, and those with positive syphilis status. Finally, primary prevention of anal HPV infections and its related diseases through HPV vaccination and secondary prevention through systematic screening of anal cancer and pre-cancerous lesions should be one of MSM health priorities in Bali, Indonesia.

DISCLOSURE

The author reports no conflicts of interest in this work.

ETHICAL CONSIDERATION

The study was approved by the institutional review board of Kerti Praja Foundation with ethical clearance No 027/IRB-YKP/2011

FUNDING

This work was supported by NIH (National Institute of Health)/President's emergency fund for AIDS relief (PEPFAR).

AUTHORS CONTRIBUTION

All of the authors equally contribute to the study from the conceptual framework, data gathering, and data analysis until reporting the study results through publication.

ACKNOWLEDGMENTS

We thank all of the staff of the Nusa Indah VCT Clinic for their help, so this study can be done.

REFERENCES

1. Forman D, de Martel C, Lacey CJ, Soerjomataram I, Lortet-Tieulent J, Bruni L, et al. Global Burden of Human Papillomavirus and Related Diseases. *Vaccine.* 2012; 30(5):F12-F23.
2. Lin C, Franceschi S, Clifford GM. Human papillomavirus types from infection to cancer in the anus, according to sex and HIV status: a systematic review and meta-analysis. *Lancet Infect Dis.* 2018;18(2):198-206.
3. Palefsky JM, Holly EA, Ralston ML, Jay N. Prevalence and Risk Factors for Human Papillomavirus Infection of the Anal Canal in Human Immunodeficiency Virus (HIV)-Positive and HIV-Negative Homosexual Men. *J. Infect. Dis.* 1998;177(2):361-7.
4. Kreutera A, Wielandb U. Human papillomavirus-associated diseases in HIV-infected men who have sex with men. *Curr. Opin. Infect. Dis.* 2009;(22):109-14.
5. Palefsky J. Human papillomavirus-related disease in people with HIV. *Curr Opin HIV AIDS.* 2009;4(1):52-6.
6. Fan S, Li P, Ouyang L, et al. Anal Human Papillomavirus Infection among MSM Attending University in China: Implications for Vaccination. *Vaccines (Basel).* 2020;8(2):175.
7. Daling JR, Madeleine MM, Johnson LG, Schwartz SM, Shera KA, Wurscher MA, et al. Human papillomavirus, smoking, and sexual practices in the etiology of anal cancer. *Cancer.* 2004;101(2):270-80.
8. Bruni L, Albero G, Serrano B, Mena M, Gómez D, Muñoz J, et al. Human Papillomavirus and Related Diseases in Indonesia Summary Report 27th July 2017. *ICO/IARC Information Centre on HPV and Cancer.* 2017. [Internet]. Available from: http://www.hpvcentre.net/statistics/reports/IDN.pdf. [Accessed on 18th February 2018].
9. Hu Y, Qian H-Z, Sun J, Gao L, Yin L, Li X, et al. Anal Human Papillomavirus Infection Among HIV-Infected

and Uninfected Men Who Have Sex With Men in Beijing, China. *JAIDS.* 2013;64(1):103.
10. Supindham T, Chariyalertsak S, Utaipat U, Miura T, Ruanpeng D, Chotirosniramit N, et al. High Prevalence and Genotype Diversity of Anal HPV Infection among MSM in Northern Thailand. *PLoS ONE.* 2015;10(5):e0124499.
11. Nowak RG, Gravitt PE, He X, Ketende S, Dauda W, Omuh H, et al. Prevalence of Anal High-Risk Human Papillomavirus Infections Among HIV-Positive and HIV-Negative Men Who Have Sex With Men in Nigeria. *Sex. Transm. Dis.* 2016;43(4):243-8.
12. Mboumba Bouassa R-S, Mbeko Simaleko M, Camengo SP, Mossoro-Kpinde CD, Veyer D, Matta M, et al. Unusual and unique distribution of anal high-risk human papillomavirus (HR-HPV) among men who have sex with men living in the Central African Republic. *PLoS ONE.* 2018;13(5):e0197845.
13. Machalek DA, Poynten M, Jin F, Fairley CK, Farnsworth A, Garland SM, et al. Anal human papillomavirus infection and associated neoplastic lesions in men who have sex with men: a systematic review and meta-analysis. *Lancet Oncol.* 2012;13(5):487-500.
14. Dong-Yan Z, Yue-Ping Y, Fu-Chang H, Jiang N, Bao-Xi W, Xiang-Sheng C. HPV Infections among MSM in Shenzhen, China. *PLoS One.* 2014;9(5):e96364.
15. Frisch M, Fenger C, van den Brule AJC, Sørensen P, Meijer CJLM, Walboomers JMM, et al. Variants of Squamous Cell Carcinoma of the Anal Canal and Perianal Skin and Their Relation to Human Papillomaviruses. *Cancer Research.* 1999;59(3):753.
16. Garbuglia AR, Gentile M, Nonno FD, Lorenzini P, Lapa D, Lupi F, et al. An anal cancer screening program for MSM in Italy: Prevalence of multiple HPV types and vaccine-targeted infections. *J Clin Virol.* 2015;72:49-54.
17. Chin-Hong PV, Vittinghoff E, Cranston RD, Buchbinder S, Cohen D, Colfax G, et al. Age-Specific Prevalence of Anal Human Papillomavirus Infection in HIV-Negative Sexually Active Men Who Have Sex with Men: The EXPLORE Study. *J. Infect. Dis.* 2004;190(12):2070-6.
18. Gallegos-Bolaños J, Rivera-Domínguez JA, Presno-Bernal JM, Cervantes-Villagrana RD. High prevalence of coinfection between human papillomavirus (HPV) 51 and 52 in Mexican population. *BMC Cancer.* 2017;17(1):531.
19. Sadlier C, Rowley D, Morley D, Surah S, O'Dea S, Delamere S, et al. Prevalence of human papillomavirus in men who have sex with men in the era of an effective vaccine; a call to act. HIV Medicine. 2014;15(8):499-504.
20. Phanuphak N, Teeratakulpisarn N, Pankam T, Kerr SJ, Barisri J, Deesua A, et al. Anal human papillomavirus infection among thai men who have sex with men with and without hiv infection: Prevalence, incidence, and persistence. *J. Acquir. Immune Defic. Syndr.* 2013;63(4):472-9.
21. Twisk DE, van der Sande MAB, van Eeden A, Heideman DAM, van der Klis FRM, de Vries HJC, et al. Detection of Incident Anal High-Risk Human Papillomavirus DNA in Men Who Have Sex With Men: Incidence or Reactivation?. *J. Infect. Dis.* 2018; 218(7):1018-26.
22. Gama A, Martins MO, Dias S. HIV Research with Men who Have Sex with Men (MSM): Advantages and Challenges of Different Methods for Most Appropriately Targeting a Key Population. *AIMS public health.* 2017;4(3):221-39.