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Co-Infection of Human Papillomavirus with Mycoplasma Hominis/Ureaplasma Urealyticum Among Female Sex Workers in Medan, Indonesia

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Abstract

Human papillomavirus (HPV) infection is one of the most prevalent sexually transmitted diseases among women aged < 35 years worldwide. Recent studies have suggested that the vaginal microenvironment influenced by bacterial infection poses for high-risk human papillomavirus (hrHPV) infection and cervical carcinogenesis. Female sex workers (FSWs) are a population susceptible to acquire Human Immunodeficiency Virus (HIV) and sexually transmitted infections (STIs), as well as transmitting the virus to others. The aim of this study is to evaluate the relationship between Mycoplasma/Ureaplasma infections and HPV infection among female sex workers. A total of 70 female sex workers of reproductive age were recruited from various location in Medan, Indonesia in 2018. Detection of Mycoplasma/Ureaplasma infections and HPV infection were obtained from PCR assessment. The results of this study showed that no correlation significant between Mycoplasma hominis/Ureaplasma urealyticum infection and HPV infection.

Introduction

Human papillomavirus (HPV) has been identified as an essential aetiology of warts, cervical intraepithelial neoplasia (CIN) and cervical cancer [1]. Among high-risk HPV, type 16 and 18 are the most carcinogenic for the progression of cervical disease and induce over 70% of cervical cancer, stated as the second most common cancer in women as reported in 2012 by the International Agency for Research on Cancer (IARC) [2]. The cervical cancer death currently accounted for about 57% of cases and 65% of cancer deaths worldwide [3], [4]. De Boer previously have stated that no information existed about the prevalence of HPV 18 or other HPV types in the Indonesian population and hypothesised that the high prevalence of HPV 18 in cervical cancer in Indonesia is caused by the high prevalence of HPV 18 in the Indonesian population [5]. The estimated incidence of cervical cancer in Indonesia is 17 per 100,000 women [6].

Beside persistent infection and an increase in viral load of HPV infection, other concomitant infections are also known risk factors causing rapid development of cervical cancer, while the negative contribution of smoking and contraceptive medication act as environmental risk factors [7]. Risk factors associated with cervical cancer include first intercourse at an early age, mutually change sexual partners, and suffering from chronic sexually transmitted infections (STIs) other than HPV and HIV [8], [9], [10].

Association between HPV infection with cervical cancer has been already known, even though several studies found Mycoplasma hominis and Ureaplasma urealyticum involvement contribute to the risk of HPV infection and the occurrence of abnormal cervical cytology [11], [12]. These bacterias were

found in 30 ± 80% women's urogenital tract as a commensal organism but had the pathogenic potential [13]. Several studies revealed that Mycoplasma hominis and Ureaplasma urealyticum played a role in developing abnormal cervical cytology associated with the development of precancerous cervical lesions [7]. Mycoplasma/Ureaplasma infections can cause chronic pelvic pain if the infection infiltrates the pelvis or genitourinary system. Persistent or untreated chronic infection can lead to cervical cancer in addition to pelvic pain, by causing persistent HPV infection or increased HPV levels [14].

Female sex workers (FSWs) are commonly known very vulnerable to exposure to HIV and sexually transmitted infections (STIs), as well as transmitting the virus or bacterias to others, due to behavioural risk factors as recurrent infections and repeated contact through high numbers of sexual partners [15]. This is compounded by the lack of knowledge and awareness of HPV infection, cervical cancer, and preventive efforts, as previously described in several studies [16], [17].

This study aims to evaluate the relationship between Mycoplasma/Ureaplasma infections and HPV infection among female sex workers in Medan, Indonesia.

Material and Methods

Study Population

This study is a descriptive study with a cross-sectional design to evaluate the relationship between Mycoplasma hominis and Ureaplasma urealyticum infection and HPV infection among female sex workers. A total of 70 female sex workers of reproductive age were recruited from various location in Medan, North Sumatera, Indonesia, between July and September 2018.

Subjects were women aged between 18 and above who were sexually active. Exclusion criteria were subjects recently diagnosed with the cervical disease within 6 months before the present study and currently pregnant. All participants were interviewed to collect information on socio-demographic background. The Ethics Committee of the University of Sumatera Utara approved the study, and informed consent forms were obtained from all subjects.

Detection of HPV and Mycoplasma/Ureaplasma

DNA samples were isolated from cervical swabs using Presto^{n} Buccal Swab gDNA extraction kit.DNA was then amplified using the established PCR method. PCR kit components used for HPV gene amplification were DNA template of 6 µl, *GoTaq*® *Green Master Mix (Promega)* of 12.5 µl, a primer of forwarding HPV. Mycoplasma hominis and Ureaplasma urealyticum used 2 primers: RNAH1 and RNAH2 that amplify the 16sRNA Mycoplasma hominis gene at 334 bp; UMS125 and UMA226 amplified Ureaplasma urealyticum serovar 3 which shows multiple bands at 403 bp for biovar 1 and 448 bp for biovar 2. The amplification mixture was carried out in 12.5 µl master mix PCR consisted of Taq polymerase enzyme, $MgSO_4$, and dNTP(Go Taq® PCR Core System, Promega).

Results

The data summarised in Table 1 showed the distribution of age according to the infection of Mycoplasma hominis/Ureaplasma urealyticum and HPV. This study showed that HPV 16 infection was higher in women aged 26-30 (12.5%), while that HPV 18 infection was found higher in women aged 18-25 (26.9%). The occurrence of Mycoplasma infections was more common in the age group 18-25 (31.4%), while Ureaplasma infections were more prevalent in the age group 31-45 (60.9%).

Table 1: Distribution of age by infection of Mycoplasma hominis/ Ureaplasma urealyticum and HPV

Infection	Total N = 70	Age in years 18-25 N = 26 (37.1%)	26-30 N = 16 (22.9%)	31-45 N = 23 (32.9%)	> 45 N = 5 (7.1%)
HPV16 (+)	3(4.3)	1(3.8)	2(12.5)	0(0)	0(0)
HPV16 (-)	67(95.7)	25(96.2)	14(87.5)	23(100)	5(100)
HPV18 (+)	13(18.6)	7(26.9)	3(18.8)	3(13.0)	0(0)
HPV18 (-)	57(81.4)	19(73.1)	13(81.3)	20(87.0)	5(100)
Mycoplasma (+)	22(31.4)	11(42.3)	5(31.3)	6(26.1)	0(0)
Mycoplasma (-)	48(68.6)	15(57.7)	11(68.8)	17(73.9)	5(100)
Ureaplasma (+)	32(45.7)	9(34.6)	6(37.5)	14(60.9)	3(60.0)
Ureaplasma (-)	38(54.3)	17(65.4)	10(62.5)	9(39.1)	2(40.0)

The previous study found that infections of *C. trachomatis*, *M. genitalicum*, and *U. parvum* were higher in the younger age group by comparisons based on age (< 50 years vs ≥ 50 years) [10]. Similar to the previous study, the respondents of this study mostly younger than 50 years, and bacterial infections more often to occur in the age group 18-25 years and 31-45 years.

Another study found that HPV infection peak in women aged 40-50 years [18]. Different from the results of the former study, HPV 16 infections were higher in women aged 26-30 years, while HPV 18 found high in women aged 18-25 years. Nevertheless, another study showed no correlation between HPV infection and the age of the respondent, and also found that age was not related to abnormal cytology or bacterial infection [19].

Table 2: Relationship between Mycoplasma hominis and Ureaplasma urealyticum infection and HPV infection

Bacterial infection	HPV 16 infection		OR	*P*-value	CI 95%	HPV 18 infection		OR	*P*-value	CI 95%
	Positive	Negative				Positive	Negative			
Mh										
Positive	0 (0,0%)	22 (32,8%)	-	0.547[a]	-	3 (23,1%)	19 (33,3%)	0.6	0.742[a]	0.148-2.440
Negative	3 (100,0%)	45 (67,2%)				10 (76,9%)	38 (66,7%)			
Uu										
Positive	2 (66,7%)	30 (44,8%)	2.426	0.589[a]	0.213-28.535	6 (46,2%)	26 (45,6%)	1.022	1.000[a]	0.305-3.422
Negative	1 (33,3%)	37 (55,2%)				7 (53,8%)	31 (54,4%)			

The results of this study as shown in Table 2, found that no correlation between Mycoplasma hominis infection with HPV 16 infection (p = 0.547) and neither with HPV 18 infection (p = 0.742). There were no correlation as well between Ureaplasma urealyticum infection with HPV 16 infection (p = 0.580), and also no correlation with HPV 18 infection (p = 0.639).

Discussion

The results were different from previous studies that found a significant association between HPV infection and the presence of Mycoplasma/Ureaplasma infection [11], [18]. Another study showed the correlation not only between bacterial infection and high-risk HPV infection but also between abnormal cytology with bacterial infection [10]. Another previous study from Korea from asymptomatic women of reproductive age with negative cytologic findings found that most HPV infections were not correlated with any specific STIs [20]. Another study from Estonia found the high risk-HPV was associated with STIs especially Chlamydia infection, and also with U. urealyticum infection in women over 41 years old. The same study found that U. urealyticum infection was not associated with HPV status [21]. A study from Nigeria found significant associations between persistent high-risk HPV infections and persistent M. Hominis in the vaginal microbiota, and the study suggested that M. Hominis may play a role in high-risk HPV induced cervical carcinogenesis [22].

Several studies showed that a high density of Ureaplasma might be associated with STIs and the differentiation of colonisation and infection contributed to co-infection, as reported by Kim et al., that showed only Ureaplasma colonization with greater than 104 CCU/mL was significantly associated with HPV infection [19]. Another study which in line showed patients with cervical lesions had higher U. parvum load colony-forming unit [23]. Unfortunately, in this study, we did not assess the bacterial load of Ureaplasma and Mycoplasma. The correlation between colonies number and infection may be explained by more pathogen colony could develop more cervical lesion as well due to chronic infections by activating the virulence factor. Few studies have been conducted to evaluate the association between ureaplasma load with cervical disorders especially with precursor cervical lesions of cervical cancer [5].

In conclusion, this study revealed that there is no significant correlation between the presence of Mycoplasma hominis/Ureaplasma urealyticum infection and HPV infection. Although among female sex workers, sexually transmitted infections like Mycoplasma spp, and Ureaplasma spp were frequently detected and as well as the HPV infection. However, this non-significant result might be due to the limitation of this study. We only recruited a small number of samples and therefore could not provide confirmed statistical significance for all of the tests performed.

References

1. Zur Hausen H. Papillomaviruses and cancer: from basic studies to clinical application. Nat Rev Cancer. 2001; 2:342-50. https://doi.org/10.1038/nrc798 PMid:12044010

2. Lee SJ, Yang A, Wu TC, Hung CF. Immunotherapy for human papillomavirus-associated disease and cervical cancer: review of clinical and translational research. Journal of gynecologic oncology. 2016; 27(5):e51. https://doi.org/10.3802/jgo.2016.27.e51 PMid:27329199 PMCid:PMC4944018

3. Hope KA, Moss E, Redman CWE, Sherman SM. Psycho-social influences upon older women's decision to attend cervical screening: A review of current evidence. Preventive Medicine. 2017; 101:60-6. https://doi.org/10.1016/j.ypmed.2017.05.002 PMid:28502577

4. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A.Global cancer statistics 2012. Cancer J Clin. 2015; 65(2):87-108. https://doi.org/10.3322/caac.21262 PMid:25651787

5. De Boer MA, Vet JN, Aziz MF, et al. Human papillomavirustype 18 and other risk factors for cervical cancer in Jakarta, Indonesia. Int J Gynecol Cancer. 2006; 16(5):1809-14. https://doi.org/10.1111/j.1525-1438.2006.00701.x PMid:17009976

6. Riskesdas. Badan Penelitian Dan Pengembangan Kesehatan Kementerian Kesehatan RI, 2013. http://www.depkes.go.id/resources/download/general/Hasil%20Riskesdas%202013.pdf. Accessed Januari 22, 2019.

7. Ji YI. Co-infections with human papillomavirus and mycoplasma/ureaplasma spp. in women with abnormal cervical cytology. Res Rep Gynaecol Obstet. 2017; 1(1):1-3.

8. Crum CP, Cibas ES, Rose PG, Peters AW, ed. Diagnostic Gynecologic and Obstetric Pathology. Vol 2. Saunders-Elsevier, 2011:245-327. https://doi.org/10.1016/B978-1-4377-0764-9.00013-5

9. Gawande V, Wahab SN, Zodpey SP, Vasudeo ND. Parity as a risk factor for cancer cervix. Indian J Med Sci. 1998; 52(4):147-50.

10. Kim HS, Kim TJ, Lee IH, Hong SR. Associations between sexually transmitted infections, high-risk human papillomavirus infection, and abnormal cervical Pap smear results in OB/GYN outpatients. Journal of gynecologic oncology. 2016; 27(5):e49. https://doi.org/10.3802/jgo.2016.27.e49 PMid:27329197 PMCid:PMC4944016

11. Biernat-Sudolska M, Szostek S, Rojek-Zakrzewska D, Klimek M, Kosz-Vnenchak M. Concomitant infections with human papillomavirus and various mycoplasma and ureaplasma species in women with abnormal cervical cytology. Advances in Medical Sciences. 2011; 56:299-303. https://doi.org/10.2478/v10039-011-

0028-9 PMid:21940266

12. Manhart LE, Critchlow CW, Holmes KK, et al. Mucopurulent cervicitis and mycoplasma genitalium. The Journal of Infectious Diseases. 2003; 187(4):650-7. https://doi.org/10.1086/367992 PMid:12599082

13. Otgonjargala B, Becker K, Batbaatar G, et al. Effect of mycoplasma hominis and cytomegalo virus infection on pregnancy outcome: a prospective study of 200 Mongolian women and their newborns. PLoS ONE. 2017; 12(3):e0173283. https://doi.org/10.1371/journal.pone.0173283 PMid:28257513 PMCid:PMC5336298

14. Lukic A, Canzio C, Patella A. Determination of cervicovaginal microorganisms in women with abnormal cervical cytology: the role of ureaplasma urealyticum. Anticancer Res. 2006; 26:4843-9.

15. Kakchapati S, Singh DR, Rawal BB, Lim A. Sexual risk behaviors, HIV, and syphilis among female sex workers in Nepal. HIV/AIDS (Auckland, N.Z.). 2017; 9:9-18. https://doi.org/10.2147/HIV.S123928 PMid:28184170 PMCid:PMC5291463

16. Kietpeerakool C, Phianmongkhol Y, Jitvatcharanun K, Siriratwatakul U, Srisomboon J. Knowledge, awareness, and attitudes of female sex workers toward HPV infection, cervical cancer, and cervical smears in Thailand. International Journal of Gynecology and Obstetrics. 2009; 107:216-9. https://doi.org/10.1016/j.ijgo.2009.07.023 PMid:19716556

17. Ersan G, Köse S, Güneş H, Özkan M. Knowledge and awareness of female sex workers towards human papillomavirus infection in Turkey. Cent Eur J Public Health. 2012; 20(3):219-22. https://doi.org/10.21101/cejph.a3738 PMid:23285524

18. Camporiondo MP, Farchi F, Ciccozzi M, Denaro A, Gallone D, Maracchioni F. Detection of HPV and co-infecting pathogens in healthy Italian women by multiplex real-time PCR. Infez Med. 2016; 24:12-7.

19. Kim SI, Yoon JH, Park DC, et al. Co-infection of ureaplasma urealyticum and human papilloma virus in asymptomatic sexually active individuals. International journal of medical sciences. 2018; 15(9):915-20. https://doi.org/10.7150/ijms.26523 PMid:30008604 PMCid:PMC6036102

20. Shim HS, Noh S, Park A, et al. Detection of sexually transmitted infection and Human Papillomavirus in negative cytology by multiplex-PCR. BMC Infectious Diseases. 2010; 10:284. https://doi.org/10.1186/1471-2334-10-284 PMid:20920170 PMCid:PMC2956726

21. Denks K, Spaeth EL, Joers K, Randoja R, Talpsep T, Ustav M. Coinfection of chlamydia trachomatis, ureaplasma urealyticum and human papillomavirus among patients attending STD clinics in Estonia. Scand J Infect Dis. 2007; 39(8):714-8. https://doi.org/10.1080/00365540701199824 PMid:17654349

22. Adebamowo SN, Ma B, Zella D, Famooto A, Ravel J, Adebamowo C, ACCME Research Group. Mycoplasma hominis and mycoplasma genitalium in the vaginal microbiota and persistent high-risk human papillomavirus infection. Frontiers in public health. 2017; 5:140. https://doi.org/10.3389/fpubh.2017.00140 PMid:28695118 PMCid:PMC5483445

23. Amorim AT, Marques LM, Campos GB, et al. Co-infection of sexually transmitted pathogens and human papillomavirus in cervical samples of women of Brazil. BMC infectious diseases. 2017; 17(1):769. https://doi.org/10.1186/s12879-017-2835-5 PMid:29246195 PMCid:PMC5732421

24. Xiaolei C, Taot H, Zongli S, Hongying Y. The role of ureaplasma urealyticum infection in cervical intraepithelial neoplasia and cervical cancer. Eur J Gynaecol Oncol. 2014; 35(5):571-5.