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Relationship between high-risk human papilloma virus (HPV) and subclinical condyloma acuminata (CA) in the cervix of high-risk women

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ABSTRACT

Condyloma acuminata (CA) is a sexually transmitted infection (STI) caused by both high- and low risk human papilloma virus (HPV) infection. Subclinical CA looks like a white spot after an acetic acid test. High-risk women are women who have a high risk of STIs, including CA. The aim of this study was to evaluate the relationship between high-risk HPV and subclinical CA in the cervix of high-risk women. This was a cross-sectional analytic study involving 30 high-risk women. The age, the age at first sexual intercourse, the frequency of sexual intercourse, the number of sexual partners and the use of condoms were recorded. Subclinical CA was diagnosed by the 5% acetowhite test. HPV infection was detected by PCR. Kruskal Wallis test was conducted to evaluate the relationship between variables and the results were considered to be significant if $p<0.05$. The HPV infection was detected in 15 high-risk women with subclinical CA and most subjects showed the high-risk type. No significant relationship between age and using of condom with high-risk HPV or with subclinical CA ($p> 0.05$). No significant relationship between age at first sexual intercourse and frequency of sexual intercourse with high-risk HPV was also observed ($p> 0.05$), however, a significant relationship with subclinical CA was observed ($p < 0.05$). In conclusion, there is a relationship between high-risk HPV and subclinical CA in the cervix of high-risk women.

ABSTRAK

Kondiloma akuminata (KA) merupakan infeksi menular seksual (IMS) yang disebabkan oleh *Human Papilloma Virus* (HPV) baik tipe risiko tinggi atau rendah. Kondiloma subklinis terlihat seperti bercak putih setelah dilakukan tes asam asetat. Wanita berisiko tinggi adalah wanita yang memiliki risiko tinggi terhadap IMS, termasuk KA. Tujuan penelitian ini adalah mengkaji hubungan antara HPV tipe risiko tinggi dengan KA subklinis pada serviks wanita risiko tinggi. Penelitian ini merupakan penelitian analitik potong lintang yang melibatkan 30 pasien wanita berisiko tinggi. Data usia, usia pertama melakukan hubungan seksual, frekuensi hubungan seksual, jumlah pasangan seksual dan penggunaan kondom dicatat. Kondiloma akuminata subklinis didiagnosis dengan tes *acetowhite* 5%. Infeksi HPV dideteksi dengan PCR. Uji Kruskal Wallis dilakukan untuk menilai hubungan antar variabel dan hubungan dinyatakan signifikan bisa nilai $p<0,05$. Infeksi HPV terdeteksi pada 15 orang (50%) wanita berisiko tinggi yang menderita KA subklinis dengan tipe risiko terbanyak, yaitu 7 orang (23,3%). Tidak terdapat hubungan nyata antara usia dan penggunaan kondom dengan infeksi HPV tipe risiko tinggi maupun KA subklinis ($p> 0,05$). Tidak terdapat hubungan nyata antara usia pertama melakukan hubungan seksual dan frekuensi hubungan seksual dengan HPV tipe risiko tinggi ($p> 0,05$), namun terdapat hubungan nyata dengan KA subklinis ($p<0,05$). Dapat disimpulkan terdapat hubungan HPV tipe risiko tinggi dengan kejadian KA subklinis di serviks pada wanita risiko tinggi.

Keywords:
condyloma acuminate;
subclinical;
high risk HPV;
PCR;
acetowhite;

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INTRODUCTION

Condyloma acuminata (CA) is a sexually transmitted infection (STI) characterized by changes in mucosal and skin hyperplasia and caused by the human papilloma virus (HPV) infection.[1] Basal cells are the first site of HPV infection after inoculation through minor trauma, HPV virions will enter the basal cell layer of the epithelium.[2] Several clinical features of CA are reported. However, subclinical form of CA that only looks like white spots (positive acetowhite) after the 5% acetic acid test performed is also reported. Therefore, the patient often goes unnoticed even undiagnosed.[1-4] This infection is also demonstrated by identification of viral DNA on genital skin.[5] Many studies estimated that subclinical HPV infection rates have a higher prevalence than clinical infections.[6,7]

High-risk women are women who have a high risk of STIs, including CA.[8] One of the groups of women at high risk of CA is female commercial sex workers.[9-11] The prevalence of CA in each country is different. In developed countries, the prevalence of CA is around 11-46%.[12] It was estimated among 122 million people aged 15-49 years in United State, more than 1% of them suffers from CA and around 2% have subclinical infection.[13] In Indonesia, the prevalence of CA ranges from 5 to 19%.[14] In Medan, North Sumatera the prevalence of CA at Haji Adam Malik General Hospital in 2008-2011 was 76 people and in 2012-2017 was 39 people.[15,16]

Based on the possibility of epithelial dysplasia and malignancy, HPV infection is divided into low-risk HPV and high-risk HPV. Low-risk HPV types, such as type 6, 11, 42, 43, 44, 54, 61, 70, 72 and 81 tend to cause benign tumors such as verrucae and CA. Meanwhile, high-risk HV types tend to cause anogenital malignant tumors, such as cervical, vulvar, vaginal, anal and penile cancers. Whereas, HPV types 16 and 18 are often found in high-grade dysplasia and malignancies.[1,17,18] A study conducted on high-risk women in Lagos showed a high prevalence of high-risk HPV types with most having one type of HPV. Age at first sexual intercourse and an increase in the number of sexual partners are the most important factors for high-risk genital HPV infection in this study.[19] A study on Italian women who have previously been diagnosed with cervical HPV showed a high risk of developing subclinical oral HPV in their sexual partners.[20] Another study in Brazil also reported that patients with genital HPV infection are at risk for oral HPV infection.[21]

The correlation between HPV infection and CA is well known. However, studies concerning high risks HPV and subclinical CA is still limited. This study was conducted to evaluate the relationship between high-risk HPV and subclinical CA in the cervix of high-risk women.

MATERIALS AND METHODS

Design of study

This was an analytic observational study with a cross-sectional design involving high risk women in Public Health Center Glugur Darat, Medan, North Sumatra from Mei 2021 to July 2021.

Protocol of study

A total of 30 high risk women whom met the inclusion and exclusion criteria were involved in this study. The inclusion criteria included high risk women and signed informed consent. According to WHO, high-risk women are those who have risk factors, including husband or sexual partner suffers from STI; husband or sexual partner or patient himself has had another sexual partner in the last one month have a new partner in the

last three month have had one or more STI episodes in the past one mo; high-risk sexual partner/husband behavior.[8] The exclusion criteria included patients who had sex, used vaginal rinses, creams and tampons the day before, patients who have a mass in the birth canal, pregnancy and breastfeeding.

The characteristics of patients included the patient's age, the age at first sexual intercourse, the frequency of sexual intercourse, the number of sexual partners and the use of condoms were recorded. Subclinical CA was diagnosed by the 5% acetowhite test, if there was a white color (positive acetowhite) on the cervix after applying 5% acetic acid.

The research samples were collected at Prodia S. Parman Laboratory in Medan, North Sumatra and would be sent to Prodia Kramat Jaya Laboratory in Jakarta to be examined for HPV types using standard PCR. The protocol of the study was approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Sumatera Utara, Medan, North Sumatra.

Statistical analysis

The collected data was tabulated and presented as frequency and percentage. The relationship between high-risk HPV types and subclinical CA in the cervix of high-risk women was statistical analyzed using the Chi Square test. If the Chi Square test conditions did not meet criteria, the Fisher's Exact test would be applied. However, if the two conditions did not meet criteria, then the Kruskal Wallis test would be applied. The results of statistical analysis were considered significant if a p value of <0.05.

RESULTS

The HPV infection was detected in 15 high-risk women with subclinical CA (TABLE 1 and 2).

TABLE 1. Distribution of subclinical CA in high-risk women after 5% acetowhite test

Subclinical CA	High-risk women
	[n (%)]
Positive	15 (50)
Negative	15 (50)

TABLE 2. Distribution of HPV infection in subclinical and non-subclinical CA

High-risk women	HPV infection	
	Positive	Negative
	[n (%)]	[n (%)]
Subclinical CA	15 (50)	0 (0)
Non-subclinical CA	0 (0)	15 (50)

Most subjects showed the high-risk type (TABLE 3). Subclinical CA was most commonly found in the 26-35 y.o. age group (7 people or 46.7%). The 12-16 y.o. age group was the first age group to have sexual intercourse with the highest number of subclinical CA subjects (9 people or 60%). The frequency of sexual

intercourse in subclinical CA subjects was mostly found in the age group with the frequency of having sex 1-7 times a wk (8 people or 53.3%). All subjects suffering from subclinical CA had more than 1 sexual partner. Subclinical CA subjects were more commonly found in the age group who had never used condoms (12 people or 80%). High risk HPV types were found in 3 people (42.9%) in the 26-35 y.o. age group, 3 people (42.9%) in the 36-45 y.o. age group and 1 person (14.3%) in the 17-25 y.o. age group. Mix of high-risk and low-risk HPV types were found in the 46-55 y.o. age group (3 people or 75%). The 12-16 y.o. age group was the first age group to have sexual intercourse with the highest number of subjects infected with high-risk HPV types (4 people or 57.1%). Mix high risk and low risk HPV types were found in 2 people (50%) in the 12-16 y.o. age group, and 2 people (50%) in the 17-25 y.o age group. Subjects with high-risk HPV types who had sexual intercourse more than once a d were found in 3 people (42.9%), 1-7 times a wk 3 people (42.9%), and the least was found in the group with the highest frequency. Having sex 1-3 times a mo was found in 1 person (14.3%). Mix high-risk and low-risk HPV types were found in 2 people (50%) in the group who had sex more than once a d, and 2 people (50%) in the group who had sex 1-7 times a wk. All subjects infected with high-risk HPV types and mix high-risk and low-risk HPV types had more than 1 sexual partner. Subjects infected with high-risk HPV types were found in the group who had never used condoms (6 people or 85.7%) and all subjects infected with mix high risk and low risk HPV types never used condoms were 4 people.

TABLE 3. Characteristics of subclinical CA in high-risk women by HPV type

HPV type	n (%)
High risk	7 (23.3)
▪ Type 16	1
▪ Type 31	1
▪ Type 45	1
▪ Type 51, 52	2
▪ Type 52	1
▪ Type 66/68	1
Low risk	2 (6.7)
▪ Type 42 and type 70	1
▪ Type 43/44	1
Mix of high risk and low risk	4 (13.3)
▪ Type 33, type 44, and type 84/26	1
▪ Type 51 and type 6	1
▪ Type 53, type 6, type 43/44, type 54/55, type 70 and type 72	1
▪ Type 58, type 53, type 40/61, and type 42	1
Outside the type found	2 (6.7)

No significant relationship between the age, number of sexual partners and use of condoms was observed ($p > 0.05$). However, a significant relationship between the age at first sexual intercourse, and frequency of sexual intercourse with subclinical CA was observed ($p<0.05$) as presented in TABLE 4.

TABLE 4. Characteristics of high-risk women based on subclinical CA infection

Characteristics of high-risk women	Sub clinical CA		p
	Positive [n (%)]	Negative [n (%)]	
Age (y.o.)			
▪ 12-16	0 (0)	0 (0)	
▪ 17-25	1 (6.7)	1 (6.7)	
▪ 26-35	7 (46.7)	9 (60)	0.510[a]
▪ 36-45	4 (26.7)	3 (20)	
▪ 46-55	3 (20)	2 (13.3)	
Age at first sexual intercourse (y.o.)			
▪ 12-16	9 (60)	2 (13.3)	
▪ 17-25	5 (33.3)	10 (66.7)	
▪ 26-35	1 (6.7)	3 (20)	0.012[a]
▪ 36-45	0 (0)	0 (0)	
▪ 46-55	0 (0)	0 (0)	
Frequency of sexual intercourse			
▪ > 1 time a d	6 (40)	2 (13.3)	
▪ 1-7 times a wk	8 (53.3)	6 (40)	0.014[a]
▪ 1-3 times a mo	1 (6.7)	7 (46.7)	
▪ < 1 time a mo	0 (0)	0 (0)	
Number of sexual partners (person)			
▪ 1	0 (0)	0 (0)	-
▪ > 1	15 (15)	15 (50)	
Use of condoms			
▪ Always	0 (0)	0 (0)	
▪ Sometimes	3 (20)	6 (40)	0.213[b]
▪ Never	12 (80)	9 (60)	

d: day; wk: week; mo: month; y.o.: years old; [a]Kruskal-Wallis Test; [b]Fisher's Exact Test

No significant relationship between the characteristics of high risk women i.e. age, age at first sexual intercourse, frequency of sexual intercourse, number of sexual partners and use of condoms with high-risk HPV was observed ($p > 0.05$) as presented in TABLE 5. Furthermore, a significant relationship between high-risk HPV and subclinical CA in the cervix of high-risk women was observed ($p < 0.05$) as presented in TABLE 6.

TABLE 5. Characteristics of high-risk women based on high-risk HPV

Characteristics of high-risk women	High risk [n (%)]	Mix of high and low risk [n (%)]	Non high-risk [n (%)]	p
Age (y.o.)				
▪ 12-16	0 (0)	0 (0)	0 (0)	
▪ 17-25	1 (14.3)	0 (0)	1 (5.3)	0.094[a]
▪ 26-35	3 (42.9)	1 (25)	12 (63.2)	
▪ 36-45	3 (42.9)	0 (0)	4 (21.1)	
▪ 46-55	0 (0)	3 (75)	2 (10.5)	
Age at first sexual intercourse (y.o.)				
▪ 12-16	4 (57.1)	2 (50)	5 (26.3)	
▪ 17-25	2 (28.6)	2 (50)	11 (57.9)	
▪ 26-35	1 (14.3)	0 (0)	3 (15.8)	0.362[a]
▪ 36-45	0 (0)	0 (0)	0 (0)	
▪ 46-55	0 (0)	0 (0)	0 (0)	
Frequency of sexual intercourse				
▪ > 1 time a d	3 (42.9)	2 (50)	5 (15.8)	
▪ 1-7 times a wk	3 (42.9)	2 (50)	9 (57.4)	0.112[a]
▪ 1-3 times a mo	1 (14.3)	0 (0)	7 (36.8)	
▪ < 1 time a mo	0 (0)	0 (0)	0 (0)	
Number of sexual partners (person)				-
▪ 1	0 (0)	0 (0)	0 (0)	
▪ > 1	7 (100)	4 (100)	19 (100)	
Use of condoms				
▪ Always	0 (0)	0 (0)	0 (0)	
▪ Sometimes	1 (14.3)	0 (0)	8 (42.1)	0.155[a]
▪ Never	6 (85.7)	4 (100)	11 (57.9)	

d: day; wk: week; mo: month; y.o: years old; [a]Kruskal-Wallis test

TABLE 6. Relationship between HPV types and subclinical CA in the cervix of high-risk women.

HPV types	Subclinical CA		p
	Positive [n (%)]	Negative [n (%)]	
High risk - Mix of high and low risk			
High risk	7 (63.6)	0 (0)	-
Mix of high and low risk	4 (34.4)	0 (0)	
Total	11 (100)	0 (0)	
High risk - Non-high risk			
High risk	7 (63.6)	0 (0)	0.001[a]
Non-high risk	4 (36.4)	15 (100)	
Total	11 (100)	15 (100)	
Mix of high and low risk - Non-high risk			
Mix of high risk and low risk	4 (50)	0 (0)	0.008[a]
Non-high risk	4 (50)	15 (100)	
Total	15 (100)	15 (100)	

DISCUSSION

There were 15 high-risk women with positive subclinical CA (50%) and 15 women (50%) who with negative subclinical CA (TABLE 1). The results of this study are in accordance with previous study that reported an abnormal cytology showing an acetowhite area on the cervix of high-risk women.[22] Several studies also reported a fairly good correlation with histopathological findings indicating HPV and the presence of positive HPV DNA in the acetowhite area.[23,24]

The HPV infection was detected in 15 people (50%) with subclinical CA and not detected in 15 people (50%) with non-subclinical CA (TABLE 2). Yanofsky *et al.*[25] reported the subclinical HPV infection rate to be 40%, whereas DNA analysis of apparently uninfected genital skin was reported to be positive for HPV. Giraldo *et al.*[26] reported that 29 people (20.7%) with CA were positive HPV infection on PCR examination.

High risk HPV type was the most detected HPV type in women with subclinical CA (7 people or 23.3%), while low risk HPV types were found in 2 people (6.7%). A mixture of high risk and low risk HPV types were found in 4 people (13.3%) and 2 people (6.7%) outside the type of HPV found (TABLE 3). Condyloma acuminata is mostly caused by HPV types 6 or 11, but can also be caused by the high-risk HPV types coinfection.[27] This study is in line with the study conducted by Hawkins *et al.*[28] that reported the presence of DNA and mRNA from one HPV type to be the cause of the development of lesions with mixed infection of high risk. In addition, low risk types was found in 4 people (33.3%) and a single infection in 8 people (66.6%). The results of this study are also in accordance with the study conducted by Al-Awadhi *et al.*[29] It was reported that high-risk HPV types were found in 34.62% of patients and low-risk HPV in 14.4 % of patients. The highest prevalence (50.6%) was HPV 1a, 2, 4, 7, 27, 57b, 57c, 65. The prevalence of HVP infection with single types, two types and triple types were 88.4%, 9.0%, and 2.6%, respectively.[29]

Subclinical CA was most commonly found in the 26-35 y.o. age group (7 people or 46.7%). However, no significantly relationship between age and subclinical CA was observed in this study (p=0.510) (TABLE 4). These results are similar to previous studies. A study conducted by Puspawati *et al.*[30] at Sanglah Hospital Denpasar, Bali reported the age of patients with CA was 12-35 y.o. Likewise, Effendi *et al.*[31] reported patients with CA who come to Dr. H. Abdoel Moeloek Distric Hospital Lampung were dominated by the 20-40 y.o. age group. Peder *et al.*[32] reported that the increase of infection risk among the young age is associated with a lack of adaptive immune response and the area of cervical epithelium. In this young age, the cervical epithelium can undergo relatively larger metaplasia in which may increase the risk of HPV infection of the basal cell layer and then increase proliferation. However, Tamer *et al.*[33] reported that the older people can suffer from CA due to decreased immunity and reactivation of latent infection.

The 12-16 y.o. age group was the first age group to have sexual intercourse with the highest people with subclinical CA (9 people or 60%). A significant relationship between the age of first sexual intercourse and subclinical CA was observed (p=0.012) as presented in TABLE 4. This result is in line with the study conducted by Tamer *et al.*[33] that reported the age at first sexual intercourse is significantly associated with the people with CA. Abnormal cells in the cervix can lead to malignancy.[33-35]

The frequency of sexual intercourse in people with subclinical CA was mostly found in the group with the frequency of having sex 1-7 times a wk (8 people or 53.3%) in this study (TABLE 4). A

significant relationship between the frequency of sexual intercourse with subclinical CA was observed (p=0.014). A study conducted by Haseen *et al.*,[36] supported the results obtained in this study. It was found that the frequency of sexual intercourse could lead to a higher positive incidence of STIs included subclinical CA. Haseen *et al.*[36] reported that adolescents who visited female sex workers at least once a mo had a higher prevalence of symptoms than other adolescents.

All subjects suffering from subclinical CA had more than 1 sexual partner (TABLE 4). Tamer *et al.*[33] reported a significant number of sexual partners in patients with CA (3 people) compared to without CA (1 people) (p = 0.0001). Peder *et al.*[32] reported that women who had multiple partners are more likely to develop CA than those had single partners.

People with subclinical CA were more higher in the group never using condoms (12 people or 80%). However, it was no significant relationship between using condom and the subclinical CA prevalence (p=0.213) as presented in TABLE 4. The results is in line with study conducted by Nareswari *et al.*[35] It was reported that the majority of people with CA informed that they had never used a condom during sexual intercourse (51.1% in men vs. 72.3% in women).[35] Many studies report the function of condoms as a protector for the prevention of transmission of HPV infection. This function is especially important in women because they do not want to be seen as distrusting their partners so that they are more susceptible to infection.[32]

High risk HPV types were found in 3 people (42.9%) in the 26-35 y.o, age group 3 people (42.9%) in the 36-45 y.o. age group and at least 1 people (14.3%) in the 17-25 y.o. age group. High-risk and low-risk mixed HPV types were found in 3 people (75%) in the 46-55 y.o. age group. No significant relationship between age and high-risk HPV types (p=0.094) was resported (TABLE 5). Kang *et al.*[37] in China reported that the prevalence of high-risk HPV types is greater in older women. The prevalence of high-risk HPV types (p<0.001), HPV16/18/45 (p=0.002), and high-risk HPV types other than HPV16/18/45 (p=0.002) generally increased with age. High-risk HPV types more found in older women due to increased lifetime exposure, incidence of HPV, and/or viral viability in older women. In addition, the high incidence in older women was due to acquired HPV infection caused by changes in the sexual behavior of women themselves and their sexual partners and reactivation of previous latent HPV infections due to a decrease in the body's immune system at menopause.[37]

The 12-16 y.o. age group was the first age group to have sexual intercourse with the highest number of subjects infected with high-risk HPV types (4 people or 57.1%). High risk and low risk mixed HPV types were found in 2 people (50%) in the 12-16 y.o. age group, and 2 people (50%) in the 17-25 y.o. age group (TABLE 5). No significant relationship between age at first sexual intercourse with high-risk HPV types was observed (p=0.362). The results of this study were not supported by Kang *et al.*[37] who reported that younger age at initiation of sexual intercourse have a higher risk of developing high-risk HPV infection.

Subjects with high-risk HPV types having sexual intercourse more than once a day were found in 3 people (42.9%), 1-7 times a wk in 3 people (42.9%), and the least were found in the group with the frequency of having sex 1-3 times a month in 1 person (14.3%). High-risk and low-risk mixed HPV types were found in 2 people (50%) in the group having sex more than once a day, and 2 people (50%) in the group having sex 1-7 times a wk. No significant relationship between the frequency of sexual intercourse with high-risk HPV

types (p=0.112) as presented in TABLE 5. Haseen *et al.*[36] reported that the more frequent the frequency of sexual intercourse will increase the incidence of STI. Adolescents who frequently visited female sex workers had more STIs than other adolescents.[36]

All subjects infected with high-risk HPV types and mixed high-risk and low-risk HPV types had more than 1 sexual partner (TABLE 5). Kang *et al.*[37] reported the most high-risk HPV types in women had a number of sexual partners 5 or more. The women who have had more than 1 sexual partner for life have a 1.3-fold risk of experiencing high-risk HPV infection.[37]

Subjects infected with high-risk HPV types were found in the group never using condoms (6 people or 85.7%) and all subjects infected with mixed high risk and low risk HPV types had never used condoms (4 people or 100%). However, no significantly relationship between using condom and high-risk HPV types (p=0.155) as presented in TABLE 5. Tay *et al.*[38] reported that women not using condoms shows a high prevalence of HPV infection (28.6%) and infection with high-risk HPV types (23.8%). In addition, the use of condoms has been shown to be protective in preventing STIs and could reduce the prevalence of HPV infection.[39]

A significantly association between high-risk HPV types and subclinical cervical CA in high-risk women (p=0.001) was observed (TABLE 6). This results are in line with the study conducted by Al-Awadhi *et al.*[29] It was reported that there is a relationship between HPV types and the incidence of CA with 34.62% of patients infected with high-risk HPV types more than 14.4% of patients infected with low-risk HPV types. Another study in Austria reported that 42% of patients are infected with low-risk HPV and 21% of patients were positive for the high-risk HPV genotype. Multiple infections with low risk and high-risk genotypes were reported in 36% of patients.[40]

Based on the possibility of epithelial dysplasia and malignancy, HPV is divided into low-risk HPV and high-risk HPV. Low-risk HPV types, such as types 6, 11, 42, 43, 44, 54, 61, 70, 72 and 81 tend to cause benign tumors such as verrucae and CA. While high risk types tend to cause anogenital malignant tumors, such as cervical, vulvar, vaginal, anal and penile cancers, where HPV types 16 and 18 are often found in high-grade dysplasia and malignancy.[1,17,18]

Cervical cancer is one of the most common types of cancer in women which it is associated with HPV infection. Patients infected with HPV genotypes 6 or 11 had an increased risk of having CA (OR=2.34; 95%CI= 0.955-5.737; p=0.06). In addition, this association increased with the presence of high-risk HPV types and low-risk HPV types for having CA (OR= 2.814; 95% CI= 1.208-6.55; p=0.017) and cases with high-risk HPV types (OR= 2,329; 95% CI= 1.029-5.269; p=0.042). Patients with CA are usually found to have CIN2/3.[41] A cohort study involving 10,971 patients (1,685 men and 9,286 women) in the Swedish population reported that CA is strongly associated with an increased risk of cancers of the anogenital tract, such as the vulva, penis, and anus.[42]

CONCLUSION

There is a relationship between high-risk HPV and subclinical CA in the cervix of high-risk women.

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