HPV 52 most dominant Human Papillomavirus (HPV)

by Muchlis Sofro

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Research Article

HPV 52 most dominant Human Papillomavirus (HPV) genotype in women infected by Human Immunodeficiency Virus (HIV) that get antiretroviral treatment (ART)

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ABSTRACT

Background:: the persistence of oncogenic or high-risk HPV infection (HPV-RT) is a causative agent of cervical cancer, a cancer with the highest prevalence in Indonesia. HIV-infected women have a higher prevalence of RT-HPV infection than HIV-uninfected women. The aim of the study was to assess the distribution of HPV genotypes in HIV-infected women who received ART.

Methods:: Analytical, cross-sectional study of 55 HIV-infected women between December 2019-March 2020 aged 24-51 years at the Dr. Kariadi Semarang and Salatiga City Hospital. HPV genotype examination method used Reserve Dot Blot "Flow-Trough" Hybridization method **Results:**: HPV DNA was detected 53%. Four samples (5.1%) could not be further categorized. 50% of respondents detected the HPV-RT genotype. The most common HPV-RT genotypes were HPV52 (7.7%), HPV68 (6.3%), and HPV66 (5.1%), whereas for low risk HPV genotypes (HPV-RR) which frequently appeared were HPV43 (6.3%), HPV44 (6.3%), and HPV6 (5.1%). **Conclusions**:: the results of this study indicate the diversity of HPV genotypes in HIV-infected women and the most dominant genotype is HPV52.

Keywords: high risk HPV, low risk HPV, genotype, HIV infected women.

INTRODUCTION

Human Papilloma Virus (HPV) is a cause of various diseases and malignancies in humans. HPV is classified into oncogenic or high risk HPV (RT-HPV) (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 59, 66, 68, and 70) and non-HPV - oncogenic or low risk (HPV-RR) (6, 11, 42, 43, 44 and 53). Type of oncogenic HPV or HPV-RT is a causative agent of cervical cancer. The main factor causing cervical cancer is not only the oncogenic HPV infection, but the most important is the persistence of the oncogenic HPV infection. One of the causes of the persistence of oncogenic HPV infection is a decrease in local immunity in the cervix, and immunosuppression as happened in patients infected with Human Immunodeficiency Virus (HIV)[2].

HIV-infected women have a higher prevalence of HPV-RT infection than those who are not infected. The immunosuppression situation faced has a high risk of cervical cancer. Data in Indonesia shows that cervical cancer is one of the cancers with the highest prevalence in 2013, one way to suppress the high rate of cervical cancer is by immunization programs, in women infected with HIV immunization is also very useful, so that this effect is effective it requires the distribution of HPV genotypes. This information is needed for the basis of vaccination, because each type of vaccine provides immunity to certain HPV genotypes[1,3–5]. The purpose of this study was to

assess the distribution of HPV genotypes in HIV-infected women receiving ART.

METHODS

This study is an analytic, cross sectional study conducted at the Central General Hospital Dr. Kariadi and the Salatiga City General Hospital in Central Java on 55 women infected with HIV between December 2019-March 2020. This study has been declared to have passed an ethical review by the Undip Community Health Research Ethics Commission Number 445 / EA / KEPK-FKM / 2019, in addition, respondents who agreed to participate in this study signed a statement of voluntary consent.

Cervical smear samples were collected in a liquid-based cytology medium (Thin rep) and sent to the Medical Laboratory with SNI ISO standard (ISO 15189: 2012). For testing HPV genotypes in December 2019-March 2020 using the Reserve Dot Blot "Flow-Trough" Hybridization Method.

HIV profile

All respondents were women who tested positive for HIV, and received ART who routinely visited outpatient services at the Dr. General Central Hospital. Kariadi and the Salatiga City General Hospital in Central Java. All respondents had received information and filled out a questionnaire, then a gynecological examination was carried out for HPV Genotype examination.

HPV Genotype

The Reserve Flow Blot "Flow-Trough" Hybridization method can detect 33 common HPV types (17 types of HPV HR (16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82) and 16 types of HPV LR (types 6, 11, 26, 40, 42, 43, 44, 54, 55, 57, 61, 70, 71, 72, 81, 84)). In this study, DNA was extracted from aliquot specimens using QIAamp DNA (Qiagen) mini kits according to manufacturer's instructions. The extracted DNA was mixed with a mixture of PCR reagents and Taq DNA Polymerase which was provided together with the GenoFlow test kit and reinforced with PCR using the thermocycling (thermal cycle) conditions stated in the guidelines. Amplicons are genotyped using Flow-through hybridization. "Flow-through" technology includes hybridization, conjugation of enzymes and colorimetry developed and intermittent washing (occasionally), which can be completed in 35 minutes. Samples will be considered valid if hybridization controls are obtained (to monitor the success of hybridization), amplification controls (for access to sample integrity or successful PCR reactions), and / or specific types of HPV on the membrane. The positivity is shown by the colored dots on the membrane, which are recorded by scanning the flat scanning membrane.

Statistic analysis

The data obtained is stored and analyzed using SPSS software and the variables are described as percentages. Data were analyzed using the Fisher's Exact Test. P values <0.05 were considered statistically significant.

Results

Demographic Data

During the study period, 60 HIV-infected female respondents who received ART were recruited, 4 of whom were absent at the examination and 1 other person did not complete the examination. Thus, respondents and samples who met the requirements and analyzed in this study were 55. Figure I. The characteristics of respondents can be seen in table 1. A total of 55 HIV-infected women who received ART were 21 years old minimum and 51 years maximum age, average age average 36 years and most age groups are more than 35 years (61.8%). The average marriage status is married or ever married (98.2%). The majority have a parity history of more than 2. On average respondents have more education than elementary school (87.3%). The majority of respondents work (56.4%).

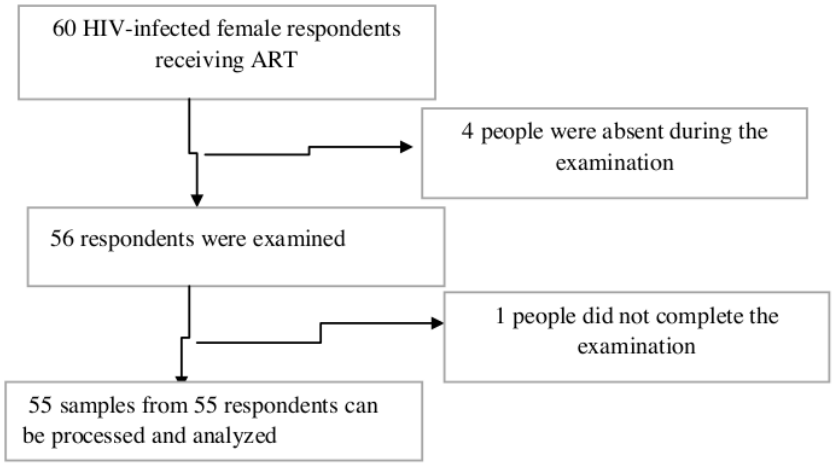

Fig.1. Flow diagram of respondents obtained and samples analyzed

Table 1:Characteristics of Respondents

Characteristics	Total (55)	HPV Status				P
		Positive		Negative		
		n	(%)	N	(%)	
Age (years)						0.375
< 35	21	10	47.6	11	52.4	
≥ 35	34	19	55.9	15	44.1	
Marittal Status						
Not married	1	1	100	0	0	0.527
Married/widow	54	28	51.9	26	48.1	
Parity Status						0.389
0-1	6	4	66.7	2	33.3	
≥ 2	49	25	51.0	24	49.0	
Education						0.168
Primary school	7	2	28.6	5	71.4	
≥ Primary school	48	27	56.3	21	43.8	
Occupation						0.534
unemployment	24	13	54.2	11	45.8	
Work	31	16	51.6	15	48.4	

Distribution of HPV Genotypes

HPV DNA was detected in 53% of respondents. Four samples (5.1%) could not be further categorized. 50% of respondents detected the HPV RT genotype. The most emerging HPV RT genotypes were HPV52 (7.7%), HPV68 (6.3%), and HPV66 (5.1%), while for the RR HPV genotypes that frequently appeared were HPV43 (6.3%), HPV44 (6.3%), and HPV6 (6.3%) 5.1%). Figure 2.

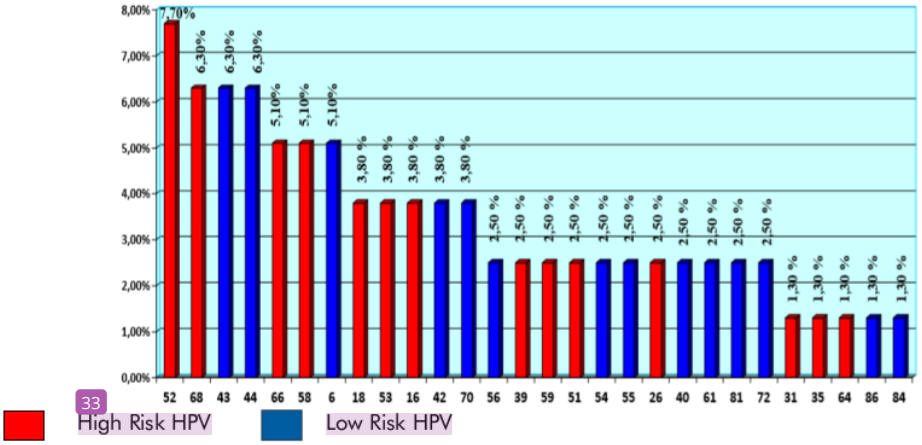

Fig.2:Distribution of HPV Genotypes

Discussion

To our knowledge, this study was the first to be carried out in Central Java in Indonesia which illustrates the distribution of HPV genotypes in HIV-infected women receiving ART. The results of this study detected HPV DNA in 53% of HIV-infected women receiving ART. This result is smaller compared to the results of other studies also conducted in Indonesia in the province of Bali in women who are also infected with HIV at 60%[6], this result is in line with other studies in Brazil which found that the prevalence of HPV in HIV-infected women is in the range of 48 % to 68%[7].

The HPV-RT genotype found was 50%. This result is in line with previous studies conducted in France which found HPV-RT around 50.1%[8] and lower than the results in Amazon which found the prevalence of HPV-RT in HIV-infected women around 61.6%[9].

The results of this study found that genotypes were very varied in all respondents, there were about 28 genotypes. The most common HPV-RT genotypes were HPV52, followed by HPV68, and HPV66. This result is in line with prior research in several Asian countries, such as Hong Kong, Shanghai, Taiwan, and Japan and also non-Asian countries such as Amazon and also in France[8–12].

In general, HPV52 ranks sixth or seventh of the most common HPV genotypes associated with cervical cancer worldwide, and the HPV genotype is most commonly found in Asia. HPV52 is the same group of species as HPV16 (alpha-9) of the genus Alphapapillomavirus. This HPV species causes 75% of invasive cervical cancers worldwide[8,9].

Another result of this study is the small number of detected HPV16s, this corroborates the results of previous studies such as research in Amazona[11,12] and Brazil[13], which states that HPV16 is not the most commonly detected genotype. Hypotheses from some experts suggest that HPV16 has a better evolutionary ability to avoid the effects of immune surveillance, while genotypes other than HPV16 are often better controlled by the body's response, immune control against species other than HPV can be lost, causing an increase in the prevalence of species that are often targeted by competent immune system[14,15].

In the study, there were no characteristic variables that were associated with respondents' HPV status, but there was something interesting to discuss here when it was associated with cervical cancer, namely age, the average age of HIV-infected women receiving ART in this study was 36 years. These results are exactly the same as the results of the characteristics of respondents conducted in Lome Togo[16] and belong to the age group where cervical cancer often occurs in Indonesia[4].

Our research has several limitations including, first, the difficulty of finding respondents, according to the researchers, is caused by local cultural socio-cultural factors, where sampling must show genital organs, for the majority of Indonesian people this is still considered taboo so prospective respondents are not pleased. Second, this research was conducted at the Hospital so that the results of this study might not describe the community. Third, the research method we use is cross sectional so in our opinion we cannot infer the cause and effect between the incidence of

HPV and the incidence of HIV, so cohort studies may be needed to be carried out in the future.
The results of this study indicate the diversity of HPV genotypes in HIV-infected women. The most dominant genotype is HPV52. The difference in the results of this study with previous research shows that this research is very important to do in each region in Indonesia so that each region has definite data related to this to formulate policies on reducing the incidence of cervical cancer, especially immunization programs, especially for women infected with HIV.

Declaration

Ethics approval and consent to participate

This study has been declared to have passed an ethical review by the Undip Community Health Research Ethics Commission Number 445 / EA / KEPK-FKM / 2019, in addition, respondents who agreed to participate in this study signed a statement of voluntary consent.

Availability of data and materials

All data are publicly available.

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Disclaimer

The funding agencies had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

Conflict of interest

All authors have not interests to declare.

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