



Correlation Between the Use of Hormonal Contraception and HPV Infection Among HIV-Infected Women

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Abstract. Cervical cancer has the potential to be prevented since the etiology is clearly known, namely the persistence of HPV infection. HPV is the cause of 99.7% of cervical cancer. There are many risk factors that can decrease cervical local immunity thereby increasing the persistence of HPV, one of which is the use of hormonal contraception. This study aims to determine the correlation between the use of hormonal contraception and HPV infection among HIV-infected women. This was a quantitative analytical study with cross sectional approach. 55 HIV-infected women found between December 2019–March 2020 and aged 24–51 years were involved as the study respondents. All respondents had been tested and confirmed positive for HIV infection, and received ART and routinely made visits to outpatient services at the Dr. Kariadi Central General Hospital and Salatiga City General Hospital in Central Java. Examination of HPV infection used the Reserve Dot Blot “Flow-Through” Hybridization method. Data on the use of hormonal contraception were obtained from direct interviews. During the study period (December 2019–March 2020) a total of 55 respondents were obtained. 29 respondents (53%) were detected to have HPV infection. Furthermore, 11 respondents (20%) used hormonal contraception. There was no correlation between the use of hormonal contraception and HPV infection among HIV-infected women (p -value = 1.000). There was no correlation between the use of hormonal contraception and HPV infection among HIV-infected women.

Keywords: Hormonal Contraception · HPV · HIV

1 Introduction

Data derived from the Global Burden of Cancer (GLOBOCAN) released by the World Health Organization (WHO) revealed that there were 18.1 million cases and 9.6 million deaths due to cancer in 2018. Cancer deaths are expected to continue to increase to more than 13.1 million in 2030. One of the most common cancers in Indonesia is cervical cancer. Data sourced from Dharmais Cancer Hospital in 2018 showed that the second most cancer case was cervical cancer at 10.69%, and it became a major contributor to all types of cancer [1, 2].

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Cervical cancer has the potential to be prevented since the etiology is clearly known, namely the persistence of HPV infection. HPV is a Deoxyribo Nucleic Acid (DNA) virus that causes proliferation on epithelial and mucosal surfaces. Such virus has many genotypes of more than 100. Based on its role in causing malignancy, there are two groups of HPV genotypes, namely high-risk HPV and low-risk HPV. HPV is the cause of 99.7% of cervical cancer. The risk of cervical cancer is increasing in immunosuppressed individuals such as among HIV-infected patients. The high prevalence of HPV among HIV-infected women can be explained by a persistent tendency to HPV, and this is in contrast to that in women who have a good immune response. There are many risk factors that can decrease cervical local immunity thereby increasing the persistence of HPV, one of which is the use of hormonal contraception [3-9]. This study aims to determine the correlation between the use of hormonal contraception and HPV infection among HIV-infected women.

2 Methods

This was a quantitative analytic study with a cross sectional approach which was conducted at Dr. Kariadi Central General Hospital and Salatiga City General Hospital in Central Java. The minimum sample in this study was 48 people who were selected based on several inclusion criteria, namely willing to be respondents in this study, infected with HIV, treated with ART, had had sexual intercourse, and in in involved in reproductive age. Sample recruitment was conducted during the period of December 2019 to March 2020, and 55 samples were eligible to be analyzed. The current study was declared to have passed the ethical review by the Health Research Ethics Commission of the Faculty of Public Health of Diponegoro University with the number 445/EA/KEPK-FKM/2019. Furthermore, the respondents who agreed to participate in this study signed a voluntary informed consent.

2.1 HIV Profile

All respondents had been tested and confirmed positive for HIV infection, and received ART and routinely made visits to outpatient services at the Dr. Kariadi Central General Hospital and Salatiga City General Hospital in Central Java. Before participating in this study, the respondents had received information beforehand and filled out a questionnaire, and further, a gynecological examination was carried out.

2.2 HPV Infection

Samples from 55 respondents in the form of cervical smears were collected in liquid-based cytology media (ThinPrep) and sent to a Medical Laboratory accredited with SNI ISO standards (ISO 15189:2012). HPV genotype test used the Reserve Dot Blot "Flow-Through" Hybridization method. Such method can detect 33 types of HPV. In this study, DNA was extracted from aliquot specimens using the QIAamp DNA mini kit (Qiagen) according to the manufacturer's instructions. The extracted DNA was mixed with the PCR reagent mixture and Taq DNA Polymerase provided with the GenoFlow assay kit

and amplified by PCR using the thermocycling conditions (thermal cycles) described in the guide. Amplicons were genotyped using Flow-through hybridization according to the manufacturer's instructions. "Flow-through" technology includes hybridization, enzyme conjugation and colorimetric developed and intermittent washings, which can be completed in just 35 min. The sample will be considered valid only if it has obtained a hybridization control (to monitor the success of hybridization), an amplification control (for access to sample integrity or a successful PCR reaction), and/or a specific HPV type on the membrane. Positive result is indicated by colored dots on the membrane, which is recorded by scanning the membrane with a flatbed scanner.

2.3 Hormonal Contraception

Data on the use of hormonal contraception were obtained from direct interviews.

2.4 Statistical Analysis

The data obtained were saved and analyzed using SPSS software and the variables were described as percentages. P value of <0.05 was considered statistically significant.

3 Results

3.1 Characteristics and HPV Infection Status of Respondents

During the study period, 60 HIV-infected female respondents who received ART were recruited, 4 of whom were not present at the examination and 1 other person did not complete the examination. Thus, 55 respondents or samples met the requirements and were analyzed in this study Fig. 1. Characteristics of respondents are presented in Table 1. The minimum age of 55 HIV-infected women who received ART was 21 years and the maximum age was 51 years. The mean age of respondents was 36 years, and most of them (61.8%) were involved in the age group of more than 35 years. Regarding marital

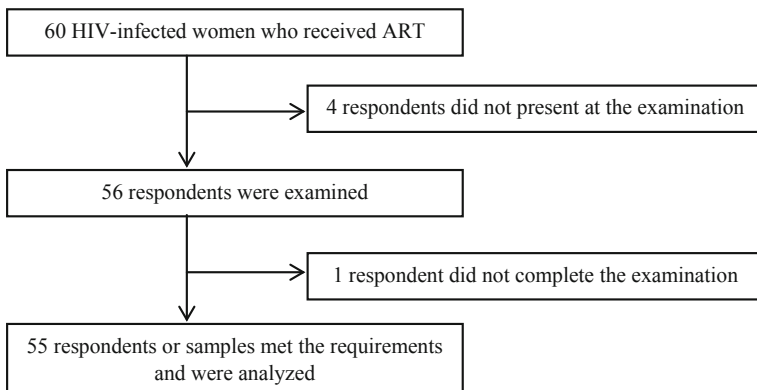


Fig. 1. Flowchart of initial number of respondents and samples to be analyzed

Table 1. Characteristics of Respondents and HPV Status

Characteristic	Total (55)	HPV Status			
		Positive		Negative	
		N	(%)	n	(%)
Age (year)					
<35	21	10	47.6	11	52.4
≥35	34	19	55.9	15	44.1
Marital Status					
Unmarried	1	1	100	0	0
Married/widow	54	28	51.9	26	48.1
Parity Status					
0-1	6	4	66.7	2	33.3
≥2	49	25	51.0	24	49.0
Education Level					
Elementary School	7	2	28.6	5	71.4
≥Elementary School	48	27	56.3	21	43.8
Employment					
Unemployed	24	13	54.2	11	45.8
Employed	31	16	51.6	15	48.4

status, most of respondents were married or ever married (98.2%). Regarding parity, the majority of respondents had more than two (2) children. The majority of respondents (87.3%) had education level of higher than elementary school. The majority of respondents (56.4%) were employed. 29 respondents (53%) were detected to have HPV infection. Complete data are presented in Table 1.

3.2 Characteristics of Respondents and HPV Status

3.3 Correlation Between the Use of Hormonal Contraception and HPV Infection Among HIV-Infected Women

The results of this study revealed that of 55 respondents, 80% used non-hormonal contraception and 20% used hormonal contraception. The finding of statistical test showed that there was no correlation between the use of hormonal contraception and HPV infection among HIV-infected women (p -value = 1.000). The complete data are presented in Table 2.

Table 2. Correlation between the use of hormonal contraception and HPV infection among HIV-infected women

Type of Contraceptive Method	HPV Status				Total		P-Value
	Positive		Negative		n	%	
	n	%	n	%			
Non-Hormonal	21	38.2	23	41.8	44	80	1,000
Hormonal	5	9.1	6	10.9	11	20	

4 Discussion

55 respondents of HIV-infected women who received ART in the study could be analyzed. The minimum age was 21 years and the maximum age was 51 years. The mean age of respondents was 36 years, and most of them (61.8%) were involved in the age group of more than 35 years. The mean age of respondents was 36 years, and most of them (61.8%) were involved in the age group of more than 35 years. Regarding marital status, most of respondents were married or ever married (98.2%). Regarding parity, the majority of respondents had more than two (2) children. The majority of respondents (87.3%) had education level of higher than elementary school. The majority of respondents (56.4%) were employed. 29 respondents (53%) were detected to have HPV infection. There were 11 (20%) users of hormonal contraception involved in this study.

This study reported that there was no correlation between the use of hormonal contraception and HPV infection among HIV-infected women (p -value = 1.000). In other words, it can be explained that the use of hormonal contraception was not a risk factor for cervical cancer. The results of this study confirm the results of a previous study conducted by Katharine et al. who also reported no conclusive correlation between the use of hormonal contraception and HPV infection. Other studies conducted by Torres Poveda, et al. and Chih, et al. also reported no correlation between the use of hormonal contraception and the incidence of cervical cancer, even hormonal contraception was reported to have a protective effect against cervical cancer [10, 11]. However, a study conducted by Dewi NK, presented contradictive finding that there was a correlation between the use of hormonal contraception and cervical cancer [12]. Goldman et al. confirmed that the use of combined oral contraceptive pills may be important in the etiology of invasive squamous cell cervical tumors if used at a critical time in women's reproductive development, namely at the age of <17 years [13]. Kuie, also found that the use of oral contraceptive pills at puberty could increase the risk of cervical cancer. Estrogen has a profound effect on the cervix during puberty and pregnancy by stimulating squamous metaplasia. The same effect was definitely found in the cervix of women who use the combined oral contraceptive pill for a long time. In theory, squamous metaplasia causes the cervix to be susceptible to carcinogenic substances [14, 15].

Respondents in this study were HIV-infected women, and most of them used condoms during sexual intercourse (data were not shown). In our opinion, the use of condoms may be one of the causes for no correlation between the use of hormonal contraception and HPV infection. This is in accordance with the opinion stated by Robboy, et al.,

that barrier contraceptive methods, one of which condoms, may be able to protect the cervical epithelium from sexually transmitted agents such as HPV in sperm. Such finding indicates that barrier contraceptive methods can reduce the risk for cervical cancer [16]. This study surely has several limitations including the cross sectional method applied which is known to be a bit inaccurate in concluding the cause and effect regarding the incidence of HPV. In addition, this study was conducted in a hospital setting so that the results may not describe the community real condition.

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