Identification of Risk Factors in Cervical Cancer

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Abstract

Background: The prevalence of cervical cancer was about 528.000 cases with mortality rate of 266.000 around the world and was ranked first as the most female genital cancers in developing countries. One of the factors suspected to be the cause of cervical cancer is the long-term use of hormonal contraception. This research aimed to identify risk factors of cervical cancer in General Hospital of Dr. Soetomo Surabaya.

Method: Analytical retrospective study with case control method was used in this study. Information about contraception use and other risk factors was obtained from personal interview. Sampling was done by *accidental sampling technique*. The sample meeting the inclusion and exclusion criteria was divided into two groups, namely 124 case groups and 124 control groups. The data was analysed using *chi-square test* and logistic regression.

Result: Patient using oral contraception for more than 5 years showed the results of OR 5.410; 95% CI = 2.403-12.176 and patient using *Intrauterine Device* (IUD) for more than 5 years had OR 3.016; 95% CI = 1.122-8.113. While prim-gravida age under 20 years was OR 2.621; 95% CI = 1.465-4.688. This data was contrast if compared with female having prim-gravida age above 20 years.

Discussion: Theoretically, the use of the hormonal contraception causes cancer. It is correlated with existence of oestrogen and progestin hormone's role to increase the protein expression of E6 and E7 from HPV. Moreover, young age is indicated to have the condition of intimal genital cells which are immature, so that if pregnancy occurs, it can induce a cell damage and facilitates genital infection.

Conclusion: The use of oral combination contraception and non-hormonal contraception more than 5 years and prim-gravida age is under 20 years are dominant factors influencing cervical cancers in woman

Keywords: *Cervical Cancer, Risk Factors, Oral Contraception, Prim-gravida*

Introduction

Cervical cancer is a global problem experienced by almost all countries in the world, particularly in developing countries. Nowadays, there are more than one million women in this world predicted to suffer cervical cancer.[1] The prevalence of it in 2012 was 528.000 cases and around 266.000 cases ended in death (7.5%) for woman. The mortality caused by cancer almost reached nine-tenth (87%) and occurred in less-developed region.[2]

The main cause of cervical cancer is often associated with infection with human papilloma virus (HPV). Human papillomavirus is a double-stranded group of viral DNA, known to be the most potential HPV types 16 and 18 to cause 70% of cervical cancer cases.[1] Various factors have been reported to be risk factors, including

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early sexual intercourse[3], sex multi-partner, smoking[4], and long-term use of hormonal contraception contributes as risk factors of cervical cancer's cause.[5]

The use of hormonal contraception is thought to cause changes in gene expression and increase the incidence of cervical cancer. A study has shown that women using oral hormonal contraception for five years or more have a greater risk of cervical cancer. [6] A systematic review notes that as many as 28 studies, including 12.531 women with cervical cancer showed that the risk of cervical cancer decreased after stopping use of oral hormonal contraception.[7] In 2005, the International Agency for Research on Cancer decided oral hormonal contraception was included in the carcinogenic classification for human uterine cervix based on clinical results, in vitro studies and experimental animals.[2]

Method

This study aimed to identify the risk factors in cervical cancer as an option to prevent this disease. An analytical retrospective study using case control design was used. Period of research was from January to October 2017.

Sample

The accidental sampling technique was used to take the sample. The total sample of the study was 252 respondents divided into two groups consisting of case and control group samples, which each amounted to 126 respondents per group. Case sample was a cervical cancer patient in the One-Stop Oncology Clinic (POSA) Dr. Soetomo. Meanwhile, the control sample was a no-cancer patient in the Gynaecology Clinic Dr. Soetomo with a number of 1:1 from the total of cases' sample.

Research Instrument and Data Analysis

Research instruments included: Data on medical records of female patients with cervical cancer in General Hospital Dr. Soetomo, informed consent and questionnaire. Data analysis used bivariate technical of chi-square test and multivariate technical of logistic regression multivariate. Statistical analysis was found to be significant if the number of p-values reached about <0.05. The data collected was processed by using SPSS program version 17. (SPSS.Inc. Chicago, IL)

Result

Distribution of Respondents Demographic

The average age in the control and case group was 47 and 52 years, with the main occupation as a housewife. Respondents, as farmers, were found more in the case group of 20 respondents (16.3%), whereas the control group were 5 respondents (4.1%). The most common type of contraception used in the case group was the combined oral pill (OCC) as many as 49 (39.5%) respondents and in the control group as many as 40 (33.1%) respondents chosen not to use contraception. (Table 1)

Results of Bivariate Analysis of Factors Affecting the Incident of Cervical Cancer

The most chosen type of contraception in the case group is OCC contraception. All contraception groups were analysed using a bivariate test and showed a p-value of 0.004 (p-value <0.05) which means that there is an influence of the use of contraception on cervical cancer events. (Table 2)

The first age to have sex in the most cases group at age <20 years was 70 respondents (56.5%) while in the control group the most had sex at the age >20 years were 79 respondents (65.3%). Bivariate test results on this variable showed a p-value of 0.001 (p-value <0.05) which meant that there was a correlation between the age of first sex with cervical cancer with an OR value of 2.438 (95% CI = 1.456-4.084).

The number of sex partners showed a difference between the case group and the control group. A total of 30 respondents (24.2%) in the case group had sex partners >1 person, whereas in the control group only 21 respondents (17.4%). Bivariate test in this variable showed a p-value of 0.189 (p-value>0.05) which meant that there was no influence between the number of partners in sex with the incidence of cervical cancer.

Bivariate testing on age of prim-gravida variable shows a p-value of 0.002 (p-value <0.05) which meant that there was an influence between the age of first pregnancy and the incidence of cervical cancer in women. Parity data of respondents in the study showed as many as 107 (86.3%) respondents in the case group had a history of parity > 2 times during life while, in the control group showed as many as 82 respondents (67.7%).

Multivariate Analysis' Result of Factors Affecting the Occurrence of Cervical Cancer

Non-hormonal contraception users >5 years have an odds ratio (OR) of 3.016 (95% CI=1.122-8.113), meaning that women who use non-hormonal contraception >5 years tend to have a risk of contracting cervical cancer 3.016 times greater than women who do not use contraception. (Table 3)

The prim-gravida age has a significant value with OR 2.621 (95% CI=1.465-4.688), meaning that women who are first pregnant less than 20 years tend to have a risk of cervical cancer 2.621 times greater than women who are pregnant when they are above 20 years old.

Based on the final results of the analysis, it can be seen that the value of Negelkerke R square is 0.165, which means that the variability of the dependent variable that can be explained by the independent variable is 16.5%, while the remaining 83.5% is explained by other variables outside the model research.

Table 1. Distribution of Respondents Demographic

Variable	**Case (n=124)**	**Control (n=121)**
	n (%)	n (%)
Age		
20-29 Years	0 (0%)	11 (9%)
30-39 Years	8 (6.4%)	22 (18%)
40-49 Years	42 (33.9%)	37 (30.7%)
50-59 Years	50 (40.3%)	24 (19.9%)
60-69 Years	21 (17%)	27 (22.4%)
70-79 Years	3 (2.4%)	0 (0%)
The number of Contraception		
Do not use	24 (19.5%)	40 (33.1%)
Combined Oral Pill	49 (39.5%)	24 (19.8%)
Injection /3months	22 (17.7%)	29 (24%)
Injection /month	4 (3.2%)	5 (4.1%)
Implant	5 (4%)	7 (5.8%)
IUD	20 (16.1%)	16 (13.2%)

Table 2. The Bivariate Analysis' Results of Factors Influencing the Incidence of Cervical Cancer

Variable	Cervical Cancer Case (n=124) n (%)	Control (n=121) n (%)	p-Value	OR (95% CI)
Contraception			0.004*	
Do not use	24 (19.5%)	40(33.1%)	REF	
Combined Oral Pill <5	7 (5.6%)	10 (8.3%)	0.782	1.167 (0.392-3.471)
Combined Oral Pill >5	42 (33.8%)	14 (11.4%)	0.000	5.000 (2.272-11.002)
Other hormonal <5	10 (8%)	15(12.4%)	0.827	1.111 (0.431-2.864)
Other hormonal >5	21 (17%)	26 (21.5%)	0.447	1.346 (0.626-2.896)
Non-Hormonal <5	6 (4.8%)	6 (5%)	0.419	1.667 (0.483-5.757
Non-Hormonal >5	14(11.3%)	10 (8.3%)	0.082	2.333 (0.897-6.072)
The First Sex Age			0.001*	2.438 (1.456-4.084)
>20 Years	54 (43.5%)	79 (65.3%)	REF	
<20 Years	70 (56.5%)	42 (34.7%)		
The Number of Sex Partners			0.189*	1.520 (0.814-2.838)
1 Person	94 (75.8%)	100 (82.6%)	REF	
>1 People	30	(24.2%)	21(17.4%)	
Prim gravida			0.002*	2.314 (1.348-3.973)
>20Years	69(55.6%)	90(74.4%)	REF	
<20 Years	55 (44.4%)	31(25.6%)		
Parity			0.001*	2.994 (1.581-5.667)
<1 times	17 (13.7%)	39(32.3%)	REF	
>2 times	107 (86.3%)	82(67.7%)		

(*) Significant result by using *p-value*<0.25

Table 3 The Multivariate Analysis' Results of Factors Influencing the Incidence of Cervical Cancer

Variable	B	p-Value	OR (95% CI)	
Contraception		0.002*		
Do Not Use		REF		
Combined Oral Pill <5	0.82	0.886	1.086	(0.354-3.333)
Combined Oral Pill >5	1.688	0.000*	5.410	(2.403-12.176)
Other Hormonal <5	0.265	0.594	1.303	(0.492-3.454)
Other Hormonal >5	0.322	0.423	1.379	(0.628-3.031)
Non-Hormonal <5	0.678	0.297	1.970	(0.552-7.033)
Non-Hormonal >5	1.104	0.029*	3.016	(1.122-8.113)
Prim gravida	0.963	0.001*	2.621	(1.465-4.688)
>20 Years		REF		
<20 Years				
Constant	-0.912			

(*) Significant result by using *p-value*<0.05

Discussion

A study conducted in 2014 showed 75% of cervical cancer sufferers were contraceptive users with the most choices, namely hormonal contraception as much as 69.2%.[8] The choice of contraception found 80 case group respondents chose to use hormonal contraception compared to 40 control group respondents who mostly chose not to use contraception. Cervical cancer patients who use oral contraception as much as 26.67%, injection contraception as much as 25.71%, IUD contraception as much as 20.95% and implant contraception as much as 3.81%.[9]

The use of contraception is often associated with the incidence of cervical cancer, specifically the use of hormonal contraception.[10] The mechanism that occurs theoretically is the role of the hormones oestrogen and / progestin to increase the expression of E6 and E7 proteins from HPV. The functions of E6 and E7 proteins themselves as degradation of tumour suppressor genes p53 and pRb.[11] The duration of contraception is often a factor in increasing the risk of cervical cancer. Risk factors will continue to increase with the length of time of exposure to hormonal contraception.[7] The effect is very weak, however, it can become stronger as the duration of use increases.[4]

There was a correlation between the age of first sexual intercourse and the incidence of cervical cancer with the results of bivariate analysis p-value = 0.001 (p<0.05). Women with the age of first sexual intercourse <20 years had an increased risk of cervical cancer by 1.75 when compared with women who have first sexual intercourse at age >20 years (95% CI=1.01-3.03). [12]

The number of sex partners is also a risk factor for cervical cancer. Cervical cancer is closely related to HPV infection. HPV is a virus that can be transmitted

through sexual intercourse whether vaginal, anal, or oral sex. The bivariate test showed the number of sex partners did not show a significant correlation to the incidence of cervical cancer with p-value = 0.189 (p>0.05).

Prim-gravida occurring in too young age is also a risk for cervical cancer. This is proved by the results of bivariate analysis that have been carried out showing a correlation between the age of first pregnancy <20 years and the incidence of cervical cancer with p-value = 0.002 (p <0.05). Most cervical cancer sufferers experience prim-gravida at the age of ≤ 18 years as many as 51 people (57.3%), whereas cervical cancer patients for those > 18 years were 38 people (42.7%).[13] Other studies conducted at Sanglah Hospital Denpasar, Bali, showed the highest incidence of cervical cancer in the 2-4 parity group of 33 people (68.8%).[14]

The variables having a significant effect on response variables were the use of OCC>5 years which meant that women who use OCC>5 years tended to have a risk of contracting cervical cancer 5.410 times greater compared to women who do not use OCC. Women using oral contraceptives for >5 years were more at risk of suffering from cervical cancer 4.17 times compared to those using oral contraceptives for less than five years or having never used oral contraceptives.[15, 16]

The use of non-hormonal contraception, the IUD, indicates meaningfulness in this study. The use of non-hormonal contraception (IUD)>5 years had an OR value of 3.016 (95% CI = 1,122-8,113) which means that women using an IUD>5 years have a risk of 3.016 times greater occurrence of cervical cancer than women who do not use contraception. Women using an IUD have a 12.7 times greater risk of cervical cancer than women who have never used an IUD before.[17]

The analysis result of the variable age for the first time pregnant showed that prim-gravida women aged under 20 years were likely to have a risk of cervical cancer 2.621 times greater than women aged over 20 years. This can be caused because pregnancy at a young age has the condition of cells in the internal genitalia of women are still too young, so that if pregnancy occurs can cause a cell damage and facilitate the occurrence of genital infections.[18] Women having prim-gravida age <20 years have a risk of 2.1 times affected by cervical cancer compared to women who are pregnant at the age of> 20-25 years (95% CI = 1.20-3.67).[12, 19]

Conclusion

The use of OCC and non-hormonal contraception for more than 5 years and the age of prim-gravida less than 20 years are two dominant factors that influenced the risk factor of cervical cancer in women.

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