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Prevalence, Age Distribution, and Risk Factors of Visual Inspection With Acetic Acid-Positive From 2007 to 2011 in Jakarta

ORIGINAL ARTICLE

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Background: Cervical cancer is still the second most frequent cancer among Indonesian women, thus screening program is still critically important to prevent it. Visual inspection with acetic acid (VIA) was introduced as a method which is most suitable with Indonesia's condition compared with the other screening methods. The Female Cancer Program from Jakarta Regional collaborated with Leiden University in 2007 to 2011 has done cervical cancer screening using VIA method, involving 25,406 women spreading across several primary health centers in Jakarta. By using these data, we found out the prevalence, age distribution, and risk factor of VIA positive in Jakarta as a basis to predict the budget and logistics for the next cervical cancer screening and to do an advocating to the Jakarta's government.
Methods: A secondary data analysis was conducted from several areas in Jakarta from 2007 to 2011. VIA test was used as the screening method, and performed by doctors and midwives with technical supervision by gynecologists.
Results: From 25,406 women, there were 1,192 cases (4.7%) of VIA test positive. The risk factors that can significantly influence the result of VIA positive were number of marriage, parity, smoking habits, and the use of hormonal contraception with OR 1.51, 1.85, 1.95, and 0.68, respectively.
Conclusions: Prevalence of VIA test-positive is 4.7% in Jakarta population. The findings of precancerous lesions and cervical cancers are not only between thirty and fifty years old, but also below the thirty years old and after fifty years old. We suggest that VIA test should be performed to all reproductive age and elder women who are not screened yet.
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Key Words: Mass screening, Uterine cervical neoplasm, Visual inspection with acetic acid

INTRODUCTION

Cervical cancer is still the 2nd most frequent cancer in women, especially in developing countries with almost 15,000 women. Cervical cancer are diagnosed every year in Indonesia and half of them died from the disease.[1-4] Therefore, screening program is still important to prevent it.

Visual inspection with acetic acid (VIA) is introduced as an alternative method that is more suitable to Indonesia's condition as it is a non-invasive, easily performed, and inexpensive method. In addition, the result can be obtained directly with a good sensitivity and specificity rates so it can be applied in all primary health care to increase the coverage of cervical cancer screening program.

The female cancer program (FCP) organization under the Faculty of Medicine, University of Indonesia–Cipto Mangunku-

sumo Hospital (FMUI–RSCM) in collaboration with University of Leiden has 'See and Treat' program that screen precancerous lesions using VIA method and simultaneously offer the immediate therapy on the first visit setting using cryotherapy. The FCP from Jakarta Regional has done cervical cancer screening from 2007 to 2011, involving 25.406 women patients spreading across several primary health centers (Puskesmas) and other agencies in several areas of Jakarta.

Using these data, we can find out the prevalence of VIA positive in Jakarta as a basis to predict the budget and logistics for the next cervical cancer screening and also a basis to do an advocating to the Jakarta's government. Besides prevalence, it is also valuable to know the risk factor that can develop the disease.

MATERIALS AND METHODS

This study was a secondary data analysis which using the data from 'See and Treat' program, that has been conducted at several areas in Jakarta from December 2007 until December 2011. 'See and Treat' program was cervical cancer screening program coordinated by FCP under FMUI–RSCM collaborated with Leiden University, and approved by the Ethics Committee of Medical Faculty of University of Indonesia (Reg. No 491/H2.F1/ETIK/ 2014). VIA was used as the screening method, and performed by general practitioners and midwives in community health centers, with technical supervision by gynecologists and management supervision by District and Provincial Health Officers. Only patients with complete data in medical record were enrolled.

We collected data from medical record, including age, educational level, history of previous cervical cancer screening, flour albus, post coital bleeding, and risk factors that can influence the result of VIA positive, such as number of marriage, parity, smoking habits, the age of first marriage, and the use of hormonal contraception. We also collected VIA result of the patient as a clinical data.

Data were analyzed using Stata ver. 10 (Stata Corp. College Station, TX, USA). We did bivariate analyzes between risk factor and VIA result. If there is more than one bivariate analysis that significantly correlated ($P < 0.25$), the study was continued with multivariate analysis. For multivariate analyzes, we gradually (stepwise) used logistic regression of prognostic models to obtain the final results that contain variables with P value less than 0.05. The value of coefficient was then displayed and the quality of the logistic regression equation was assessed as an assessment of the ability of calibration and discrimination. Homer and Lemeshow test assessed the ability of the calibration and the ability of

discrimination was assessed by the value of area under the curve (AUC) generated by receiver operating characteristic.

RESULTS

From December 2007 until December 2011, there were 25,406 women screened with VIA. Demographic data are shown in the Table 1. From 25,406 women, 83.1% were in the the reproductive age (20-49 years) with a median of 38 years and the most recent education is senior high school or bachelor degree (62.5%). More than a third (36.5%) had suffered from vaginal discharge.

There were 1,192 cases (4.7%) women with positive VIA results of which 1,162 cases (97.5%) have area of acetowhite lesion <75% and were thereby eligible for treatment with cryotherapy. A total of 4,745 cases (18.7%) women had cervicitis and 19 cases (0.08%) women had cervical cancer. From 1,192 cases of women with positive VIA result, a total of 534 cases (44.8%) are in the range of age 30-39 years, 303 cases (25.4%) are in the range of age 40-49 years, and surprisingly 25.0% of VIA positive are in the range of age 20-29 years (Fig. 1).

Bivariate analyzes using chi-square test revealed that more than one risk factor significantly correlated ($P < 0.05$) with VIA result, such as the number of times the women had been married, parity, smoking habits, and the use of hormonal contraceptives with OR 1.51 (95% CI, 1.22-1.86), 1.85 (95% CI, 1.640-2.089), 1.95
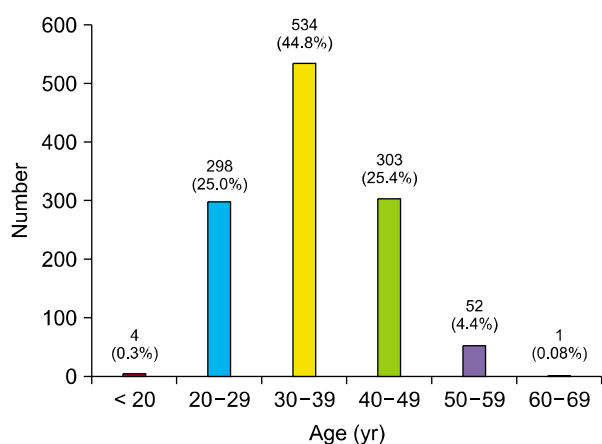
Table 1. Demographic characteristic

Demographic characteristic	Number (%)
Total Age (yr)[a]	25,406 (100)
<20	85 (0.3)
20-29	4,460 (17.6)
30-39	9,382 (36.9)
40-49	7,247 (28.5)
50-59	3,398 (13.4)
60-69	763 (3.0)
≥70	71 (0.3)
Educational background	
Illiteracy	188 (0.7)
Primary school	4,206 (16.6)
Junior high school	5,134 (20.2)
Senior high school/bachelor degree	15,878 (62.5)
History of pap test	
Ever	4,181 (16.5)
Never	2,1225 (83.5)
History of flour albus	
Positive	9,245 (36.4)
Negative	16,161 (63.6)

[a]Median age (range) = 38 years (13-89 years).

(95% CI, 0.37-0.71), and 0.68 (95% CI, 0.60-0.76), respectively (Table 2).

The results of logistic regression showed that significantly correlated ($P < 0.05$) variables with VIA result are number of marriages, parity, smoking habits, and the usage of hormonal contraceptive. The strength of the correlation from the strongest to the weakest are smoking habits (OR, 2.02; 95% CI, 1.461-2.778), parity (OR, 1.93; 95% CI, 1.713-2.186), the number of marriages (OR, 1.47; 95% CI, 1.190-1.813), and hormonal contraceptives (OR, 0.64; 95% CI, 0.567-0.722) (Table 3). Using equation $y = $ constant $+ a_1x_1 + a_2x_2 + a_3x_3 + a_4x_4 + a_ix_i$ and with the value of constant -3.344, a stands for value of coefficient for each variable, and x stands for risk factor, therefore the logistic regression equation was revealed as $y = -3.344 + 0.384$ (number of marriage) $+ 0.660$ (parity) $+ 0.701$ (smoking habits) -0.446 (hormonal contraceptive). The P-value of Hosmer and Lemeshow test was 0.102 showing that the equation has realtively good ability of calibration and the ability of discrimination of the equation was in weak category based of the value of AUC that was only 61% with sensitivity and specificity 76% and 40%, respectively.

Figure 1. Visual inspection with acetic acid positive proportion according to age distribution.

Table 2. Association of risk factors and VIA result

Variable	VIA (+) (n=1,192)	VIA (−) (n=24,195)	P-value[a]	OR	95% CI
Number of marriage					
> 1x	99 (8.3)	2,914 (12.0)	0.001*	1.51	1.22-1.86
1x	1,093 (91.7)	21,281 (88.0)			
Parity					
≥ 2	739 (62.0)	18,186 (75.2)	0.001*	1.85	1.64-2.08
< 2	453 (38.0)	6,009 (24.8)			
Age of first marriage (yr)					
≥ 20	883 (74.1)	17,749 (73.4)	0.604	0.97	0.85-1.10
< 20	309 (25.9)	6,447 (26.6)			
Smoking habits					
(+)	43 (3.6)	457 (1.9)	0.001*	1.95	0.37-0.71
(−)	1,149 (96.4)	23,738 (98.1)			
Hormonal contraceptive					
Yes	732 (61.4)	12,531 (51.8)	0.001*	0.68	0.60-0.76
No	460 (38.6)	11,664 (48.2)			

Values are presented as number (%). VIA, visual inspection with acetic acid. [a]Test with chi-square. *The result was statistically significant.

Table 3. Multivariate analysis of logistic regression

Variable	Coefficient	OR	SE	Z	P-value	95% CI
Number of marriage	0.384	1.47	0.107	12.800	0.001*	1.190-1.813
Parity	0.660	1.93	0.062	112.764	0.001*	1.713-2.186
Smoking habits	0.701	2.02	0.164	18.278	0.001*	1.461-2.778
Hormonal contraceptive	−0.446	0.64	0.062	52.580	0.001*	0.567-0.722
Constant value	−3.344					

*The result was statistically significant.

DISCUSSION

From demographic characteristics, 83.1% of women who participated cervical cancer screening program were in the range of age 20-49 years with a median of 38 years due to most of the women married in the age of early 20 years and joined the program at the age above 20 years.

The prevalence of VIA test positive was 4.7%, with most of the cases (97.0%) had an area of acetowhite lesion < 75%. Area of acetowhite lesion needs to be determined in order to decide whether the patients can have subsequent management, such as cryotherapy or not. The prevalence of VIA positive from the range of age 20-29 years is quite high (25.0%) that can be used as an additional data for further policy enforcement on the targeted group of age for cervical cancer screening in Indonesia.

In the medical record, there is no data about the number of sexual partners and the age when first sexual intercourse happened. It may be because the influence of cultural factors in Indonesia, namely senses of hesitation for giving the right information related with it. If the question is still forced to be asked, there will be high biased information. Then we took the existing data (Table 2) and the most adjacent to the risk factors, such as the number of marriages and the age of first marriage, even though we realized that the number of marriages can not be equated with risk factors for having more than one sexual partner, and the age of first married can not be equated with the age when first sexual intercourse happened. The dependent variable that we used was VIA result. In the precancerous lesions, the process is only limited to changes in the degree of differentiation epithelium so that it can be cured.

A total of 8.3% of women with VIA positive have a number of marriage more than once. These variables significantly correlated ($P < 0.05$) with VIA results with OR 1.51 (95% CI, 1.22-1.86), which means that patient had a risk of 60% for getting the VIA positive if she had been married more than once. Our study has a consistent result with previous study conducted in Jakarta. It was concluded that women who had more than one sexual partner had ORs of 5.83 (95% CI, 2.98-11.36) on the incidence of VIA positive cervical cancer.[5]

From de Boer et al.'s[5] study, it was known that women with parity more than 3 could increases the risk of cervical cancer (OR, 2.7; 95% CI, 1.55-4.72). Our study is quite consistent that women with number of children as much as 2 or more had OR 1.85 (95% CI, 1.640-2.089) which means that women with these risk factors had a risk about 64.0% for getting the VIA positive. Multiparity may result in cumulative trauma or immunosuppressive effects

against the cervix, thus facilitating the occurrence of human papilloma virus (HPV) infection. Another mechanism is the influence of hormonal factors during pregnancy towards transformation zone of the cervix so that it will increase the exposure of HPV infection or hormonal changes that affect the immune response.[6,7]

Women who had first sexual intercourse above the age of 20 years could reduce the risk of cervical cancer with ORs of 0.48 (95% CI, 0.28-0.85).[4] The age of first marriage was not significantly correlate ($P > 0.05$) with VIA positive results.

A multivariate study conducted by de Boer et al.[5] in Jakarta showed that smoking was not significantly correlated with cervical cancer. However, our study indicated that smoking habits was significantly correlated with VIA result with OR 1.95 (95% CI, 0.37-0.71). Prospective study conducted by Giuliano et al.,[8] showed that smoking habits can promote carcinogenic process by increasing the duration of oncogenic HPV infection and decreasing clearance rate of HPV infection. In this study, there is data about intensity, duration, and the number of packs of cigarettes annually. Those smoking behavior parameter need to be known as one of the studies by Haverkos et al.[9] suggests that the risk of cervical cancer increases with the increase in number of cigarettes but is not related to the length of smoking habits.

Several studies have shown an association between cervical cancer and duration of hormonal contraceptive usage (oral pill and injection), especially when it is used more than 5 years.[10-12] However, from our study, hormonal contraceptives seems to have a protective effect that significantly correlate ($P < 0.05$) with VIA result with OR 0.68 (95% CI, 0.60-0.76). The differences may be due to duration of hormonal contraceptive usage, not the unavailability of data on medical record.

Multivariate analysis revealed the equation y = −3.344 + 0.384 (number of marriage) + 0.660 (parity) + 0.701 (smoking habits) −0.446 (hormonal contraception). The equation can be applied to predict the probability of someone to obtain a positive VIA results, using the formula $P = 1 / (1 + e^{-y})$. The highest probability value about 16.9% in patients with risk factors for a number of marriage more than once and parity ≥ 2 have a smoking habits. The lowest probability value about 2.26% in patients with a number of marriages only once and parity < 2, don't have smoking habits but use hormonal contraceptive.

In conclusion, the prevalence of positive VIA test in Jakarta from December 2007 to December 2011 was 4.7%. There is statistically significant relationship between risk factors, such as the number of marriage, parity, smoking, and hormonal contraception on the incidence of precancerous lesions, characterized
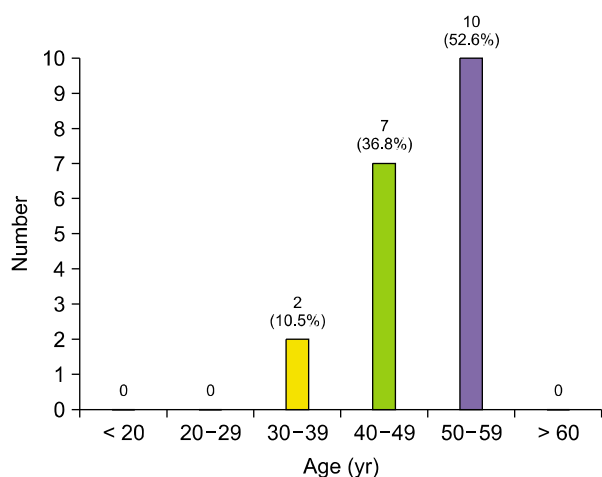
Figure 2. Cervical cancer cases proportion according to age distribution.

by the positive results of the VIA. History of hormonal contraceptive use has a value of OR of 0.68 ($P < 0.05$) on the incidence of precancerous lesions. The risk factor of age of first marriage has no statistically significant relationship to the occurrence of precancerous lesions. We proposed that implementation of early detection of cervical cancer is not limited to the age between 30 and 50 years. This is because we found the VIA positive result 25.3% before the age of 30 years and suspected cervical carcinoma 52.6% and VIA positive result 4.4% above the age of 50 years (Fig. 2).

CONFLICTS OF INTEREST

No potential conflicts of interest were disclosed.

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