Biomoleculer Screening on Women\Risked Servical Cancers in Medan North Sumatera

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Abstract: Cervical cancer is a women's health problem in Indonesia with the first order with high mortality. Effective screening that can be used is Papanicolau Tests (Papsmears) to detect precancerous lesions and immunohistochemistry techniques to identify the image of cervical cancer gene triggers in women at risk of cervical cancer.This study aims to see biomolecular screening on women risked cervical cancers in Medan North Sumatera.This study used cross sectional design. Samples were taken by consecutive sampling technique. The number of samples taken as many as 80 samples, divided into 2 groups of 40 samples were examined papsmears and 40 samples were examined immunohistochemistry technique.Pap smears from risk factors such as 72.5% of respondents were age group more than 35 years and 37.5% the results of papsmears not normal, 97.5%married respondents with abnormal 47.8% papsmears results, 67.5% were unemployed with abnormal 35% pap smears results, 62.5% of respondents with regular women's menstrual cycles with an abnormal 30% papsmears, 75% of respondents with a history of not using contraception with a majority of abnormal papsmears of 37.5%. immunohistochemistry technique from risk factors such as age of over 35 years had IHC +1 (7.5%) and IHC +3 (2.5%), married status (87.5%) with HC +1 (7.5%) and IHC +1 (2.5%) result IHC +1 have high school education (5%), Diploma (2.5%) and IHC +3 (2.5%), with status not working with IHC +1 (5%), and IHC +3 (2.5%), history parity has the same distribution of ≤ 2 and 2 with 45% sample with female parity status with IHC intensity 0 and parity ≤ 2 with IHC intensity +1 (2.5%) and IHC intensity +3 (2.5%), with regular menstrual cycle with IHC +1 result (5%), and irregular menstrual cycle with IHC +3 (2.5%), non-FP (30%) result, with FP Mantap of IHC +1 (5%) and FP Hormonal with IHC +3 (2.5%).

1 INTRODUCTION

Cervical cancer in developed countries ranks fourth after breast cancer, colorectal and endometrium, while in developing countries ranks first (Kemenkes RI, 2015). Various risk factors have been identified to increase the risk of cervical cancer, namely; sexual intercourse, patner characteristics, gynecological history, diethylstilbesterol (DES), infectious agents, Human Papilloma Virus (HPV), Herpes Simplex Virus, smoking. Some other predicted risk factors increase the risk of cervical cancer, namely: oral contraceptives, diet, ethnic and social and occupational factors (Imam, 2009). Human Papilloma virus as the cause of cervical cancer is found in 99.7% of cases of cervical cancer. It is the WHO reason to set HPV 16 and 18 to be a carcinogen agent in humans.

Cancer cells are the accumulation of a number of genetic changes that contribute to the incidence of tumorigenesis, tumor progression and resistance to chemotherapy. Most of these genetic changes result in cell cycle regulation. Loss of some molecular checkpoints, found in the development of some tumors, is because of cell cycle progression that becomes dysregulated. The accumulation of genetic changes contributes to the onset of chemoresistance resulting in the ability of DNA to respond to damage. Detectable DNA damage is regulated by a 53 p Suppressor tumor, when the DNA damage is severe enough p53 to initiate a cell death program (apoptosis) (Calvagna, 2007).

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2 METHOD

This study used a cross sectional research design with research design by measuring or observing research subjects simultaneously or once. The population of this study women at risk of cervical cancers. The sample was taken by consecutive sampling technique that is the sample selection by setting the subject according to the inclusion criteria in the research until the sample quantity is fulfilled. The research was conducted at Bhayangkara Hospital Medan, the location of this study was taken because the general hospital in the city of Medan and have women at high risk of cervical cancer both in terms of age, hormone contraceptive use. The study duration is one year.The number of samples taken as many as 80 samples, divided into 2 groups of 40 samples were examined papsmear and 40 samples were examined Immunohistochemical technique.

After getting permission from the hospital, the researcher collected the data. The first stage of data collection of prospective respondents are classified as: married and sexually active women, gynecological history of more than two children, use of diethylstilbesterol (DES), smokers or passive smokers, body weight, use of oral contraceptives.Then the cotton biopsy sample was taken for pap smear and IHC examination. After the data of all actions done finished then continued by comparing the data of pap smear and IHC examination results.

The Research Ethics Committee from the Commission of Health Research Ethics Faculty of Nursing University of Sumatera Utara No. 1154/IV/SP/2017. The data was analyzed using univariat so that just gotten the frequency distributions.

3 RESULT

Table 1 shows that most (72.5%) of the samples are age group over 35 year old and the majority of normal and abnormal papsmears at age >35 year old is 37.5%. Table 2 shows that most (70%) of the samples are age group over 35 year old having negative intensity 0 (negative p53) and 7.5% intensity +1 (p53 negative) and 2.5% intensity +3 (P53 positive or protein expression p 53 over expression). Table 3 shows that most (97.5%) of samples with marital status married with a majority result of abnormal pap smear 47.5%. Table 4 shows that most of the samples with married marriage status (87.5%) with the majority of IHC results with intenistas 0 (negative P53) and 7.5% IHC +1 results (negative p53) and 2.5% with IHC +3 results (P53 positive or protein expression p 53 over expression). Table 5 shows that most (50%) women with senior high school education degree with a majority of pap smear are abnormal at 25%. Table 6 shows that most of the samples (90%) with IHC results of intensity 0 (negative P53) have senior high school (42.5%), Diploma (15%), Bachelor (32.5%) and IHC results of intensity +1 (negative p53) (5%), Diploma (2.5%) and IHC +3 results (positive p53 / over p53 expression) of (2.5%). Table 7 shows that most (67.5%) with status not working with abnormal Paps Smear results of 35%.

Table 1. Frequency distribution by age of women with Pap Smear

age (years)	frequency sample	percentage sample	frequency abnormal pap smear	percentage normal pap smear	frequency abnormal pap smear	percentage abnormal pap smear
<20	0	0	0	0	0	0
20-35	8	20	5	12.5	5	12.5
>35	32	80	15	37.5	15	37.5

Table 2. Frequency distribution by age of woman with IHC

IHC results	<20 years	% sample	20-35 years	% sample	>35 years	% sample	total	total % sample
0	0	0%	8	20 %	28	70%	36	90%
+1	0	0%	0	0%	3	7.5%	3	7.5%
+2	0	0%	0	0%	0	0%	0	0
+3	0	0%	0	0%	1	2.5%	1	2.5%

Table 3. Frequency distribution by marriage status of women with PapSmear results

marital status	frequency sample	percentage sample	frequency abnormal pap smear	percentage normal pap smear	frequency abnormal pap smear	percentage abnormal pap smear
Married	39	97.5	20	50	19	47.5
divorced/ widowed	1	2.5	0	0	1	2.5

Table 4. Frequency distribution by marriage status of women with IHC results

IHC result	merried	% sample	Divorced/ widow	% sample	total	total % sample
0	35	87.5%	1	2.5 %	36	90%
+1	3	7.5%	0	0%	3	7.5%
+2	0	0%	0	0%	0	0%
+3	1	2.5%	0	0%	1	2.5%

Table 5. Frequency distribution by marriage status of women with IHC results

educational degree	frequency sample	percentage sample	frequency abnormal pap smear	percentage normal pap smear	frequency abnormal pap smear	percentage abnormal pap smear
senior high school	20	50	10	25	10	25
diploma	7	17.5	2	5	5	12.5
bachelor	13	32.5	8	20	5	12.5

Table 6. Frequency distribution by status of education of women of reproductive age with IHC results

IHC results	senior high school	% sample	diploma	% sample	bachelor	percentage sample	total	total % sample
0	17	42.5 %	6	15%	13	32.5%	36	90%
+1	2	5%	1	2.5%	0	0%	3	7.5%
+2	0	0	0	0%	0	0%	0	0%
+3	1	2.5%	0	0%	0	0%	1	2.5%

Table 7. Frequency distribution based on women employment status with Pap Smear results

employment status	frequency sample	percentage sample	frequency abnormal pap smear	percentage normal pap smear	frequency abnormal pap smear	percentage abnormal pap smear
working	13	22.5	7	17.5	6	15
not working	27	67.5	13	32.5	14	35

Table 8. Frequency distribution based on women employment status with IHC results

IHC results	labor	% sample	not working	% sample	total	total % sample
0	12	30%	24	60%	36	90 %
+1	1	2.5 %	2	5 %	3	7.5 %
+2	0	0 %	0	0 %	0	0 %
+3	0	0 %	1	2.5 %	1	2.5 %

Table 9. Frequency distribution by women Parity with Papsmear results

Parities history	frequency sample	percentage sample	frequency abnormal pap smear	percentage normal pap smear	frequency abnormal pap smear	percentage abnormal pap smear
≤ 2	20	50	7	17.5	13	32.5
>2	20	50	13	32.5	7	17.5

Table 10. Frequency distribution by women parity with IHC results

IHC results	≤ 2	% sample	>2	% sample	total	total precentage sample
0	18	45 %	18	45 %	36	90%
+1	2	5%	1	2.5%	3	7.5%
+2	0	0%	0	0%	0	0%
+3	0	0%	1	2.5%	1	2.5%

Table 11. Frequency distribution based on women menstrual cycle with Papsmear result

menstrual cycle	frequency sample	percentage sample	frequency abnormal pap smear	percentage normal pap smear	frequency abnormal pap smear	percentage abnormal pap smear
regularr	25	62.5	13	32.5	12	30
irregular	12	30	5	12.5	7	17.5
not menstruation	3	7.5	2	5	1	2.5

Table 12. Frequency distribution based on women menstrual cycle with IHC results

IHC results	regular	% sample	irregular	% sample	not menstruation	% sample	total	total % sample
0	24	60 %	9	22.5 %	3	7.5%	36	90%
+1	1	2.5 %	2	5 %	0	0%	3	7.5%
+2	0	0 %	0	0	0	0%	0	0%
+3	0	0 %	1	2.5 %	0	0%	3	7.5%

Table 13. Frequency distribution based on women menstrual cycle with IHC results

FP history	frequency sample	percentage sample	frequency abnormal pap smear	percentage normal pap smear	frequency abnormal pap smear	percentage abnormal pap smear
hormonal FP	5	12.5	2	5	3	7.5
Simple FP	0	0	0	0	0	0
IUD	3	7.5	2	5	1	2.5
mantap FP	2	5	1	2.5	1	2.5
not using FP	30	75	15	37.5	15	37.5

Table 14. Frequency distribution based on FP history with IHC results

IHC results	Hormonal FP	% sample	IUD	% sample	mantap FP	% sample	not using FP	% sample	total	% total sampel
0	4		2		0		30		36	
+1	0	0 %	1	2.5%	2	5%	0		3	
+2	0	0 %	0		0		0		0	
+3	1	2.5%	0		0		0		1	

Table 8 shows that most samples (60%) with status not working with IHC intensity 0 (negative p53) and 5% with IHC intensity +1 (negative p53) of 5%, and IHC +3 results (positive P53) of 2.5%. Table 9 shows that the history of parity has the same distribution of ≤ 2 and> 2 with 50% of the sample with the parity status of women with an abnormal number of papsmear of 32.5 in the history of parity ≤ 2. Table 10 shows that the parity history has the same distribution of ≤ 2 and >2 with 45% of the sample with female parity status with IHC intensity 0 (negative p53) and parity ≤ 2 with IHC intensity +1 (negative p53) of 2.5% and IHC result +3 intensity of 2.5%. Table 11 shows that most (62.5%) of samples with regular women's menstrual cycles with an abnormal number of pap smear are 30%. Table 12. demonstrated that most (60%) samples with regular menstrual cycles with IHC intensity 0 (negative protein p53), and 2.5% samples with regular menstrual cycles with IHC +1 (negative p53), and 5% samples with irregular menstrual cycles with IHC +1 results (negative p53), and 2.5% of samples with irregular menstrual cycles with IHC +2 results (negative p53). Table 13 shows that most (75%) respondents with not FP history with a majority of paps mear are abnormal on 37.5%. Table 14 shows that most of the samples are not using FP (30%) with a result of IHC intensity of 0 (negative p53) and a sample with the mantap FP of 5% with IHC +1 (negative p53), and a Hormonal FP sample with IHC +3 result of (2.5%).

4 DISCUSSION

In the results of this study found that the majority of samples> 35 years. In adult women over 35 years old, the condition of the reproductive organs begins to aging, and in theory it is explained that the risk factors that can increase the incidence of women with cervical cancer are premenarche and post menopause (Baradero & Dayrit, 1998). Generally new mucosal cells mature after women aged 20 years and over. When a woman has sex at adolescence, It is the most vulnerable done under the age of 16 years.

This is related to maturation of mucosal cells in the cervix. At a young age mucosal cells in the cervix are not yet mature and that means are still susceptible to stimulation, so they are not ready to receive stimulation from the outside, including chemical substances that brought sperm. Because it is still susceptible, mucosal cells can change the nature of cancer. But when sex is done after the age of 20 years in which mucosal cells are no longer too susceptible to changes. HPV infection is influenced by age factor and immune condition, both of these factors affect false positive values. False positive values are positive HPV DNA testing but after other tests such as colposcopy, IVA and papsmear, no cervical cancer is found. women over 30 years of age are more likely to have an exact or persistent HPV infection (Novel, Safitri, & Nuswantara, 2009).

The results of this study was the majority of samples married status. This is in accordance with the theory that married women increase the risk of cervical cancer due to sexual behavior. Cervical cancer can occur because of sexual activity, because at the time of sexual intercourse the woman can enter the female reproductive organs that can cause infections that if not treated immediately can become cervical cancer after several years later (Lisnawati, 2013).

Women who are sexually active at the age of 20-35 years and infected by HPV will suffer from cervical cancer in the 10-20 year period and married women before the age of 20 years will be at risk of cervical cancer because at that age the reproductive organs are not ready to have sexual intercourse at early age (Smeltzer & Bare 2002), but women who

are slow to marry are also risk factors for cervical cancer because these women will continue to ovulate without interruption so that stimulation of the endometrium occurs continuously so that it can make endometrial cells change the nature into cancer cells.

The results of this study obtained the majority with the results of papsmear and abnormal IHC at most with the level of senior secondary education. Acceptance of new behavior will be easier if based on the correct knowledge, awareness and positive attitude (Notoatmodjo & Soekidjo, 2012). Increased knowledge will not always cause behavioral changes, Lack of knowledge that causes poor perineal behavior of hygiene can have an impact on the increasing incidence of cervical cancer. Lack of knowledge in maintaining vaginal hygiene and correct attitude about maintaining cleanliness and lack of information leads to a lack of new knowledge gained so that the behavior of vaginal hygiene becomes dependent on the environment (Nurhayati & Annisa, 2013).

The results of this study were obtained mostly with the status of not working.Factory income related to nutrition and immunity. Low income groups generally have less quantity and quality of food and this affects the body immunity. The strong relationship between the incidence of cervical cancer with low socioeconomic level. Low-income groups are usually less accessible with quality health services including pap smear examination should be done women aged 35 years and over. Low-income women usually do not pay attention to nutritional status and immunity. Income is very influential on the incidence of cervical cancer. Low income is difficult to implement individual hygiene, sanitation and maintenance of health is lacking. According to Styarini (Setyarini & Tjakraatmadja, 2009), there is a relationship between cervical cancer with income, where women with low incomes are 4 times more at risk than high-income women.

The results of this study found that the history of parity has the same distribution that is ≤ 2 and> 2. Based on research results Hidayat, Hasibuan, and Fitriyati, (2014). that the parity of more than>3 16.03 times the risk of cervical cancer than people who have the number of parity <3. Women with high parity are associated with the evolution of cervical columnar epithelium during pregnancy which causes a new dynamic of immature metaplastic epithelium that can increase the risk of cell transformation and trauma to the cervix, making it easier for HPV infection (Center for Disease Control and Prevention Human Papillomavirus-Associated Cancer United State, 2008).

Hormone changes during pregnancy are likely to make women are more susceptible to HPV infection or cancerous growth. In this study most experienced regular menstruation and the majority of abnormal papsmear as much as 30%. Irregular menstruation can be caused by hormonal balance disorders.

The results of this study with non-family history with papsmear and abnormal IHC. Taking more than 5 years of birth control pills containing progesterone and estrogen has a bad effect on the uterus, which is an infection of the uterus and allows a woman to have uterine cancer (Wahyuningsih & Mulyani, 2014).

It can be concluded that the use of contraception has an effect on cervical cancer. Oral contraceptives with high estrogen levels cause adhesions of Candida albicans which are the bacteria that cause flour albous. Candida albicans can cause adhesions to the vaginal epithelium and is a medium for fungal growth. Candida albicans develops well in pH 5-6.5 environments, these changes can be asymptomatic or cause infection.

Some journals also mentioned that the use of mouthwashes such as chlorhexidine, benzydamine, sodium bicarbonate, granulocyte macrophage colony-stumulating factor (GM-CSF) showed ineffectiveness in reducing the degree of mucositis. The use of chlorhexidine for a long time can cause tooth discoloration and damage to mucous membranes.

5 CONCLUSION

1) Most percentage (72.5%) of samples were age group over 35 years and the majority of normal and abnormal pap smear at age> 35 years was 37.5%.
2) Most percentage (97.5%) of samples with married status married with majority result of abnormal pap smear 47.5%.
3) Percentage of the majority (50%) of women with high school education with the majority of abnormal papsmear by 25%
4) Most percentage (67.5%) with status not working with abnormal pap smear results of 35%.
5) The percentage of parity history has the same distribution that is ≤2 and> 2 with 50% sample with parity status of women with the majority of abnormal pap smear of 32.5 in the history of parity ≤2.
6) Most percentage (62.5%) of samples with regular women's menstrual cycles with an abnormal pap smear majority of 30%.

7) The percentage of most (75%) respondents with a history of non-FP with a majority of abnormal pap smear of 37.5%.
8) The percentage of most (70%) samples were age group over 35 years had IHC intensity 0 (negative p53) and 7.5% intensity +1 (p53 negative) and 2.5% intensity +3 (P53 positive or protein expression p 53 over expression).
9) The percentage of married marriage status (87.5%) with majority result of IHC with intenistas 0 (negative P53) and 7.5% result of iHC +1 (negative p53) and 2.5% with result of IHC +3 (P53 positive or protein expression p 53 over expression).
10) The percentage of sample (90%) with IHC intensity 0 (negative P53) high school (42.5%), Diploma (15%), Bachelor (32.5%) and IHC intensity +1 (negative p53) high school (5%), Diploma (2.5%) and IHC +3 Result (positive p53 / over p53 expression) of (2.5%).
11) The percentage of sample (60%) with status not working with resultIHC intenistas 0 (negative p53), and 5% with result of IHC intensity +1 (negative p53) 5%, and result of IHC +3 (positive P53) equal to 2.5%.
12) The percentage of samples with parity history had the same distribution of ≤2 and 22 with 45% sample with female parity status with IHC intensity 0 (negative p53) and parity ≤ 2 with IHC intensity +1 (negative p53) of 2.5% and IHC intensity +3 result of 2.5%.
13) The percentage of sample (60%) with regular menstrual cycle with IHC intensity 0 (negative protein p53), and 2.5% samples with regular menstrual cycles with IHC +1 (negative p53), and 5% samples with irregular menstrual cycles with results IHC +1 (negative p53), and 2.5% sample with irregular menstrual cycle with IHC +2 result (negative p53).
14) The percentage of sampel was immune (30%) with result of IHC intensity 0 (negative p53) and sample with FP steady at 5% with result of IHC +1 (negative p53), and Hormonal family planning sample with IHC +3 result (2.5%).

6 SUGGESTIONS

1) Increasing education activities and health promotion about cervical cancer prevention by holding seminar or examination of cervical cancer detection either Pap smear, IV examination or IHC examination.
2) For the community to all women play an active role in the prevention of cervical cancer is to follow the cervical cancer seminar and early detection of cervical cancesr examination.
3) For women who have ever done cervical cancer should re-do periodically at least once a year if obtained the results are normal and check the repeat is to do a six-monthly examination.

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