Factors Associated with Breast Cancer in Women of Reproductive Age at Dr. Pirngadi Hospital, Medan, North Sumatera

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ABSTRACT

Background: Breast cancer has the highest prevalence in Indonesia. The objective of the research was to analyze the risk factors which influenced the incidence of breast cancer in women of reproductive age.

Subjects and Method: This was a case-control study conducted at Dr. Pirngadi Hospital, North Sumatera. The population was all 15-49 year-old breast cancer women. Sample of 42 women of reproductive age with breast cancer and 42 women without breast cancer was selected for this study. The dependent variable was breast cancer. The independent variables were family history of breast cancer, menarche, history of breastfeeding, and history of fibrocystic disease. The data were collected by questionnaire and medical record. The data were analyzed by a multiple logistic regression.

Results: History of family with breast cancer (OR= 4.93; 95% CI=1.33 to 18.28), age of menstruation (OR= 8.46; 95% CI=2.34 to 30.64), history of breastfeeding (OR= 8.46; 95% CI= 2.19 to 32.70), and history of fibrocystic disease (OR= 7.12; 95% CI=1.99 to 25.48) were associated with breast cancer.

Conclusion: History of family with breast cancer, age of menstruation, history of breastfeeding, and history of fibrocystic disease are associated with breast cancer.

Keywords: breast cancer, history of breastfeeding, women of reproductive age

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BACKGROUND

The incidence of cancer increased from 12.7 million cases in 2008 to 14.1 million cases in 2012, with the number of deaths increasing from 7.6 million people in 2008 to 8.2 million in 2012. Cancer is the second leading cause of death. 13% in the world after cardiovascular disease (Kemenkes RI, 2014).

Breast cancer is the second most common cancer in the world and is the most common cancer in women. In 2008, breast cancer caused 458,503 deaths worldwide (13.7% of cancer deaths in women). In 2011 more than 508,000 women died from breast cancer. In 2012, an estimated 16.7 million new cases of breast cancer were diagnosed (25% of all cancers). Breast cancer was more prevalent in less developed areas (883,000 cases) than in more developed areas (794,000 cases). The incidence of breast cancer in East Asia in 2011 was recorded at 18 per 100,000 women, Southeast Asia 26 per 100,000 women, West Asia 28 per 100,000 women and Central Asia 22 per 100,000 women (GLOBOCAN and Elattar, 2011).

Breast cancer is the type of cancer with the highest prevalence in women in Indonesia. This cancer can be found at an earlier stage, but nowadays cancer is more often recognized at an advanced stage (70%) so that the mortality rate is high. If it is found at an earlier stage, it can reduce mortality and save very high health financing (Ministry of Health, 2017).

Based on estimates from Globocan, the International Agency for Research on Cancer (IARC) in 2012, the incidence of cancer in women in Indonesia is 134 per 100,000 population with the highest incidence in women is breast cancer at 40 per 100,000 followed by cervical cancer 17 per 100,000 and colorectal cancer 10 per 100,000 women. The death rate in Indonesia for breast cancer is 16.6 deaths per 100,000 population. Based on the Hospital Information System (SIRS) in 2010, inpatient cases of breast cancer were 12,014 cases (28.7%) (Ministry of Health, 2016).

Patient data at Dharmais Cancer Hospital Jakarta in 2010-2015 revealed that breast cancer ranked first in the last 10 years to 2016. In fact, there is an increase every year, the proportion of breast cancer is around 40% of all cancer cases in the hospital (Ministry of Health, 2016).

Based on the Health Profile of North Sumatra (2016), the number of women aged 30-50 years was 319,180 people, of which the tests carried out for cervical cancer and breast cancer were 13,560 people (4.25%). The results showed that 113 people had tumors (0.04%), while 285 people had positive IVA (0.09%).

Dr. Pirngadi Hospital Medan is one of the referral hospitals in the city of Medan, North Sumatra. Based on the results of the preliminary survey conducted at the Dr Pirngadi Medan Hospital, it was shown that the number of breast cancer patients was increasing every year. In 2016 the number of breast cancer patients was 240 people. From 2017 to October the number of breast cancer patients had reached 171 people. This shows that the number of breast cancer patients who come for treatment at the Dr. Pirngadi Medan Hospital tends to increase.

SUBJECTS AND METHOD

1. Study Design
This was an analytical study with a case control design. It was conducted at Dr. Pirngadi Medan Hospital from February to August 2018.

2. Population and sample
The population in this study were all women aged 15-49 years who suffered from breast tumors at Dr. Pirngadi Medan Hospital. The population in this research will be divided into a case group and a control group. The case population is all women aged 15-49 years who have a tumor in the breast area with the results of a biopsy or histopathological examination suffering from breast cancer at Dr Pirngadi Medan Hospital. The control population was all women aged 15-49 years who had tumors in the breast area with the results of biopsy or histopathological examinations and no signs of malignancy at Dr Pirngadi Medan Hospital. The sample was taken based on the case control research formula in the sample using OR family history of 2.8 so that the number of samples obtained was 42 for the case group and 42 for the control group with a ratio of 1: 1.

3. Study Variables
The dependent variable was breast cancer. The independent variables were family history, age at first menstruation, gestational age of first child, history of breastfeeding, use of contraception, breast lumps, high fat diet, exercise, smoking and alcoholic drinks.

4. Operational Definition of Variables

The breast cancer was breast tumor with the results of a biopsy or carcinoma histopathological examination recorded at the Dr. Pirngadi Medan Hospital.

Family history refers to the respondent's family suffering from breast cancer.

The age of menarche was the age at which the respondent first experienced menstruation.

Age at the first pregnancy was the age at which the respondent first got pregnant.

Breastfeeding was the activity of breast-feeding by the women after giving birth for up to six months (exclusive breastfeeding).

Contraceptive use was defined as the use of hormonal contraceptives by women of childbearing age.

A history of breast lumps was a breast tumor that the respondent had experienced before.

High-fat foods were the amount of fat consumed by respondents in one day, calculating the amount of fat (vegetable and animal) consumed.

Sport was counting the number of times the respondent does exercise in one week, the length of doing it and the continuity or greater than four times a week with a duration of approximately 30 minutes.

Smoking was a community habit in consuming cigarettes, calculated by the number (sticks) of cigarettes smoked in each day. Smoking habits were grouped into two groups, namely non-smoking and smoking (<12 cigarettes / day or ≥12 cigarettes / day (Eason, 2005).

Alcoholic drinks were drinks that contain alcohol.

5. Study Instruments

Primary data were obtained through direct interviews with respondents consisting of breast tumor patients with a positive biposi or histopathological cancer as a case and breast tumor patients with biposi or benign lesion histopathology as a control.

The data obtained were obtained from a study of documents at the DrPirngadi Medan Hospital.

6. Data Analysis

Data related to descriptive descriptions of each variable were analyzed using univariate analysis. Bivariate analysis using a simple regression test was conducted to determine whether there was an influence between the independent variables and the incidence of breast cancer in women of childbearing age. Multivariate analysis was carried out to see the effect of the independent variables with the dependent variable and which independent variable had the greatest influence on the dependent variable. Multivariate analysis was performed using multiple logistic regression.

RESULTS

A. Sample Characteristics

The number of respondents in this study were 42 cases and 42 controls. Table 3 shows that the largest number of respondents was in the 25-34 years age group in the case group, namely 13 people (31.0%) and the 35-44 years old in the control group as many as 22 people (52.4%). Characteristics of respondents based on education where the largest group of respondents is with high school education in the case group as many as 22 people (52.4%) and those with tertiary education for the control group are as many as 26 people (61.9%).

Table 1. Characteristics of Respondents by Age and Education

Variable	Case		Control	
	n	%	n	%
Age				
15-24	9	21.4	4	9.5
25-34	13	31.0	7	16.7
35-44	12	28.6	22	52.4
>45	8	19.0	9	21.4
Education				
Primary School	3	7.1	0	0
Junior high school	4	9.5	3	7.1
Senior high school	22	52.4	13	31.0
College	13	31.0	26	61.9

Table 2. Frequency Distribution of Factors Affecting the Incidence of Breast Cancer in Women of Fertile Age at Dr Pirngadi Hospital, Medan

Risk Factors	Case		Control	
	n	%	n	%
1. Family History				
Yes	25	59.5	7	16.7
No	17	40.5	35	83.3
2. Age at the first menstruation				
< 11 years	30	71.4	11	26.2
≥11 years	12	28.6	31	73.8
3. Age at first pregnancy				
< 20 years	19	45.2	8	19.0
≥ 20 years	23	54.8	34	81.0
4. History of breastfeeding				
< 6 months	33	78.6	18	42.9
≥ 6 months	9	21.4	24	57.1
5. The use of contraception				
> 10 years	25	59.5	13	31.0
≤ 10 years	17	40.5	29	69.0
6. History of breast lumps				
Yes	28	66.7	12	28.6
No	14	33.3	30	71.4
7. High Fat Food				
Yes	22	52.4	13	31.0
No	20	47.6	29	69.0
8. Sport				
No	15	35.7	10	23.8
Yes	27	64.3	32	76.2
9. Smoking				
Yes	4	9.5	3	7.1
No	38	90.5	39	92.9
10. Consuming alcohol				
Yes	3	7.1	2	4.8
No	39	92.9	40	95.2

Table 3. Types of Fatty Foods Consumed by Respondents

Type of Food	Case		Control	
	n	%	n	%
Fried food	7	31.2	3	23.1
Fast food	10	45.5	5	38.5
Meatball	5	22.7	5	38.5

Table 4. Smoking Behavior

Smoking Behavior	Case		Control	
	n	%	n	%
< 12 sticks	3	7.1	3	7.1
≥ 12 sticks	1	2.4	0	0
Pasive smokers	25	59.5	20	47.6
Non smoker	13	30.9	19	45.2

B. Bivariate Analysis

The results of Chi square showed that breast cancer was affected by family history, age at menarche, age at first pregnancy, history of breastfeeding, use of contraception, breast lumps, high-fat foods, and exercise.

Table 8. Risk Factors that Affect the Incidence of Breast Cancer in Women of Fertile Age at Dr Pirngadi Medan Hospital

Risk Factors	Case		Control		OR (95% CI)	p
	n	%	n	%		
1. Family History						
Yes	25	59.5	7	16.7	7.35	<0.001
No	17	40.5	35	83.3	(2.65-20.37)	
2. Age at menarche						
< 11 years	30	71.4	11	26.2	7.045	<0.001
≥11 years	12	28.6	31	73.8	(2.70-18.40)	
3. Age at first pregnancy						
< 20 years	19	45.2	8	19.0	3.51	0.012
≥ 20 years	23	54.8	34	81.0	(1.31-9.36)	
4. History of breastfeeding						
< 6 months	33	78.6	18	42.9	4.89	0.001
≥ 6 months	9	21.4	24	57.1	(1.89-12.74)	
5. The use of contraception						
> 10 years	25	59.5	13	31.0	3.28	0.010
≤ 10 years	17	40.5	29	69.0	(1.34-8.06)	
6. History of breast lumps						
Yes	28	66.7	12	28.6	5.00	0.001
No	14	33.3	30	71.4	(1.98-12.64)	
7. High Fat Food						
Yes	22	52.4	13	31.0	2.45	0.048
No	20	47.6	29	69.0	(1.01-5.98)	
8. Sport						
No	15	35.7	10	23.8	1.78	0.235
Yes	27	64.3	32	76.2	(0.69-4.60)	
9. Smoking						
Yes	4	9.5	3	7.1	1.37	0.694
No	38	90.5	39	92.9	(0.29-6.53)	
10. Consuming alcohol						
Yes	3	7.1	2	4.8	1.54	0.647
No	39	92.9	40	95.2	(0.24-9.71)	

C. MultivariateAnalysis

Based on the results of the simple logistic regression test that had been carried out, 8 (eight) variables were obtained, namely family history, age at first menstruation, age at first pregnancy, history of breastfeeding, use of contraception, history of breast lumps, high-fat foods and exercise (p= 0.250) so that the eight variables can be continued to the multivariate analysis. The multivariate test carried out is multiple logistic regression, as follows:

Table 9. Effect of family history, age at menarche, age at first pregnancy, history of breastfeeding, use of contraception, history of breast lumps, high-fat diet and exercise on the incidence of breast cancer in women of childbearing age at Dr Pirngadi Hospital, Medan

Independent Variables	OR	95% CI		p
		Lower limit	Upper limit	
Family History	4.93	1.33	18.28	0.017
Age at the first menstruation	8.46	2.34	30.64	0.001
Breastfeeding history	8.46	2.19	32.70	0.002
History of breast lumps	7.12	1.99	25.48	0.003
Constant	0.02			<0.001

Based on the results of multiple logistic regressions, it shows that the most dominant variable affecting the incidence of breast cancer in female women at Dr Pirngadi Medan Hospital is the variable of breastfeeding history with an OR value of 8.46 (95% CI 2.190 - 32.697).

Population Attributable Risk (PAR) with the following formula:

$$PAR = \frac{p(r-1)}{p(r-1)+1} x$$

p= 0,78

$$PAR = \frac{0,78(8,462-1)}{0,78(8,462-1)+1} x = 85\%$$

The result of PAR value in the history of breastfeeding is 85%, meaning that 85% of breast cancer incidence in women of childbearing age can be prevented by improving risk factors, namely a history of breastfeeding.

DISCUSSION

1. The relationship of family history and breast cancer

The results of this study indicate that there is an influence between family history and the incidence of breast cancer in women of childbearing age. Women with a family history of cancer were 4.93 times more likely to develop breast cancer than people without a family history of cancer.

This is in line with Rianti et al. (2012) which stated that there was an effect of family history on the incidence of breast cancer (OR= 6.44; 95% CI= 2.9 to 13.9; p= 0.001). Mothers who have a family history of breast cancer have a 6.44 times higher risk of developing breast cancer compared to mothers who do not have a family history of breast cancer.

The results of this study are in accordance with the statement of Lanfranchi (2005) which states that women who have relatives who suffer from breast cancer will have a higher risk of breast cancer, especially siblings, brothers or sisters or daughters.

Study by Sun (2017) states that a woman, whose mother or sister has breast cancer, will be very susceptible to developing breast cancer in the future. This trend is thought to be due to breast cancer-related gene mutations such as BRCA1 and BRCA2.

The results of this study are consistent with Kapoor et al. (2020) related to genetic loci and the role of the IGFBP5 gene and

the estrogen pathway in the development of hereditary breast cancer.

2. The relationship between the age of menarche and breast cancer

The results of this study indicated that there was an effect between the age of menarche and breast cancer (OR= 8.46; 95% CI= 2.34 to 30.64; p= 0.001). Women who have menarche age <11 years have an 8.46 times risk of suffering from breast cancer compared to people who have menarche age ≥11 years. This study is in line with Momenimovahed and Salehiniya (2019) which examined 11,890 women in China who stated that earlier age at first menstruation was closely related to breast cancer.

However, this study contradicts the study by Bretnall et al. (2018) after evaluating risk factors for 10 years and stated that the age at first menarche, the lower the risk of experiencing breast cancer, was around 12-13 years.

This result is in line with the research of Rianti et al. (2012) which stated that there was an effect of the age at first menstruation with the incidence of breast cancer (OR= 6.68; 95% CI= 2.9 to 15.9; p= 0.001). Mothers who have a history of first menstruation <12 years have a 6.68 times higher risk of suffering from breast cancer compared to mothers who have a history of menstrual age ≥ 12 years.

For women who have their first period at age <12 years, the duration of estrogen exposure is longer and the risk of developing breast cancer is slightly higher. When a woman has her first period, the ovarian cycle functions to produce estrogen begin. The amount of estrogen and progesterone exposure a woman has during her lifetime is believed to be a risk factor. The longer a woman is exposed, the regularity of the menstrual cycle also plays a role. The regu-larity of the cycle describes the frequency of exposure (Lanfranchi, 2005).

3. The relationship between the gestational age of the first child and breast cancer

The results of the bivariate analysis showed that there was an effect of the gestational age of the first child with the incidence of breast cancer in women of childbearing age where the (p= 0.012), so it was followed by a multivariate analysis. The results obtained after conducting multiple logistic regression tests were p = 0.644.

This is not in line with research conducted by Rianti, Tirtawati and Novita (2012) and Ardiana, et al. (2013) which states that there is an effect of the first pregnancy age with the incidence of breast cancer (OR= 2.33 (95% CI= 1.0 to 5.2; p= 0.04).

4. The relationship between history of breastfeeding and breast cancer

The results of this study indicated that there was an influence between the history of breastfeeding on breast cancer (OR = 8.46; 95% CI = 2.19 to 32.70; p = 0.002). Women who had a history of breastfeeding <6 months had an 8.46 times risk of developing breast cancer compared to people who had a history of breastfeeding ≥ 6 months. A history of breastfeeding is the most dominant factor influencing the incidence of breast cancer.

This is in line with Priyanti et al. (2013) who showed that a history of breast-feeding is risky (not breastfeeding) (OR= 2.12; 95% CI= 0.36 to 12.32). Women who have never breastfed have a 2.12 times higher risk of developing breast cancer than women who have never breastfed. This condition is influenced by hormonal mechanisms. Women who are breastfeeding will secrete a hormone called prolactin. In the body, the prolactin hormone will suppress exposure to the hormone estrogen in large

amounts and for a long time which can lead to breast cancer (Anothaisintawee et al., 2013).

This study is also in accordance with the study of Anstey et al. (2017) which states that the history of breastfeeding in mothers is related to hormonal changes and changes in molecular histology in the breast which can reduce the risk of individual breast cancer.

5. The relationship between contraceptive use against breast cancer

The results of this study indicate that there is no effect between history of contraceptive use and the incidence of breast cancer in women of childbearing age.

This is not in line with Prabandari and Fajarsari (2016) which states that there is an influence between the use of hormonal contraceptives and the incidence of breast cancer at Dadi Keluarga hospital, Purwokerto. This study is also inconsistent with the research of Lee et al. (2018) who stated that exogenous hormonal (such as use of oral contraceptives) and the use of postmenopausal hormonal replacement therapy can increase the risk of developing breast cancer.

6. The relationship history of breast lumps and breast cancer

The results of this study indicated that there was an effect between breast lumps and the incidence of breast cancer in women of childbearing age (OR = 7.12; 95% CI = 1.99 to 25.48; p = 0.003). Women who have a history of lumps in the breasts are 7.12 times more likely to develop breast cancer than women who do not have a history of lumps in the breasts.

These results are in line with Rianti et al. (2012) which states that there is an effect of a history of benign tumors on the incidence of breast cancer. Indrati's research (2005) shows that there is a significant effect between a history of benign tumors

and the incidence of breast cancer (OR= 4.38; 95% CI= 1.14 to 16.77; p= 0.020), meaning that women who suffer from breast cancer are 4.38 times likely to have a history of benign tumors in the breast. compared with women without benign tumors.

An increased risk of developing breast cancer in women with a history of benign tumors associated with an excessive proliferation process. The existence of an excessive proliferation process of breast tissue without the control of cell death programmed by the process of apoptosis will result in malignancy due to the ability to detect DNA damage.

7. The relation of consumption of high-fat foods and breast cancer

The results of this study indicate that there is no effect between consumption of high-fat foods with the incidence of breast cancer in women of childbearing age.

This is not in line with Indrati (2005) which states that there is an effect of fat consumption patterns on the incidence of breast cancer (OR= 3.5; 95% CI= 1.52 to 8.04; p= 0.003). Women who have breast cancer are 3.5 times more likely to have a history of high fat consumption than people without breast cancer.

The results of this study are also inconsistent with Khodarahmi et al. (2015) which states that an increase in the total consumption of fat and certain types of fat in the diet is associated with an increased risk of breast cancer in adult women.

8. The relationship between exercise and breast cancer

The results showed that there was no effect between exercise and the incidence of breast cancer in women of childbearing age.

There was no effect of exercise on the incidence of breast cancer in this study, perhaps due to the high consumption of high-fat foods in the case and control

groups, so that the physical activity carried out by the respondents helps burn fat tissue which is the site of the formation of the hormone estrogen which can trigger breast cancer.

9. The relationship between smoking and breast cancer

The results of bivariate analysis performed using simple logistic regression test obtained p value = 0.694, meaning that there was no effect between smoking and breast cancer incidence in women of childbearing age, so the smoking variable could not be continued to a multivariate analysis.

This study is not in line with Indrati (2005), regarding passive smoking which has an effect on the incidence of breast cancer (OR= 2.36; 95% CI= 1.08 to 5.19; p= 0.003), meaning that people who are exposed to secondhand smoke or second-hand smoke are at risk. 2.36 times higher than non-passive smokers.

This result is also not in line with Li et al. (2015) which states that exposure to secondhand smoke in secondhand smoke increases the risk of breast cancer and there is a dose-dependent significance between how long secondhand smoke has been and the risk of cancer.

The results of this study are also inconsistent with the study conducted by Maas et al. (2018) which states that lifestyle risk factors including smoking increase a woman's risk of developing breast cancer.

10. The relationship between alcohol consumption and breast cancer

The results of this study indicate that there is no effect between alcohol consumption and the incidence of breast cancer in women of childbearing age.

This result is in line with the research of Nurhayati (2015), which states that there is no effect of alcohol consumption history on the incidence of breast cancer.

Even so, this study is not in line with the results of the study by Mc Donald et al. (2014) there is a significant relationship between alcohol consumption in postmeno-pausal women on the incidence and recurrence of breast cancer.

Research that has been done on the factors that influence the incidence of breast cancer in women of childbearing age in Dr. Pirngadi Medan can be concluded that the risk factors that can influence the incidence of breast cancer in women of childbearing age are family history, mens-trual age, history of breastfeeding and a history of breast cancer.

AUTHOR CONTRIBUTION
Mila Trisna Sari, Sorimuda Sarumpaet, and Fazidah Aguslina Siregar collect the data, did data analysis, interpreted the result of data analysis, and wrote the manuscript.

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