

Risk Factors and Probability of Breast Cancer in Women in West Sumatera: A Case-Control Study

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ABSTRACT

Breast cancer is the most common cancer and the leading cause of cancer death among women worldwide. Most cases of breast cancer are in developing countries. In Indonesia, the number of new cases of breast cancer and deaths from breast cancer is among the highest among other countries in Southeast Asia or ASEAN. This study aims to assess the risk factors and probability of breast cancer in women in West Sumatra. This research is quantitative research with a case-control study design through a retrospective approach using a questionnaire instrument. The sample size obtained was 100 women with breast cancer (case sample) and 100 women without breast cancer (control sample) (1:1), so the total sample was 200 people. Data were analyzed bivariate using chi-square test, and multivariate using logistic regression test. The results of the logistic regression test were also used to estimate the probability of a woman getting breast cancer by calculating the equation. The results of the bivariate analysis revealed that the factors that were significantly associated with the risk of breast cancer were family history ($p=0.001$, OR=5.05: 95% CI, 1.82-14.00), age ($p=0.001$, OR=1.99: 95% CI, 1.06-3.38), age of menarche ($p=0.034$, OR=1.83: 95% CI, 1.045-3.207), age of first childbearing ($p=0.001$, OR=6.39: 95% CI, 2.52-16.24), parity ($p=0.022$, OR=2.14: 95% CI, 1.10-4.15), breastfeeding history ($p=0.001$, OR, 4.16: 95% CI, 1.96-8.83), oral contraceptives ($p=0.044$, OR, 1.88: 95% CI, 1.01-3.49), passive smoking ($p=0.023$, OR=2.27: 95% CI, 1.10-4.65), and fruit consumption ($p=0.035$, OR=2.00: 95% CI, 1.04-8.65). Meanwhile, menopausal age, physical activity, vegetable consumption, and BMI were not associated with breast cancer because the p -value > 0.05 . The results of multivariate analysis showed that age, family history of breast cancer, age of giving birth to their first child, and history of breastfeeding were the most important risk factors for the occurrence of breast cancer. The most dominant factor was the age of giving birth to the first child ($p = 0.001$, Exp (B) = 6.16, 95% CI = 2.33–16.28, B value = 1.818). Based on logistic regression tests and equation calculations, it is known that the probability of a woman getting breast cancer is 76.46% if she has 4 risk factors for multivariate results, namely age > 50 years, there is a family history of breast cancer, age at first childbirth > 30 years and never breastfeeding/breastfeeding < 12 months. This study shows that breast cancer risk factors among women in West Sumatra are strongly related to genetic, reproductive, and lifestyle factors. Therefore, it is necessary to provide health education to women about risk factors for breast cancer, and periodic examinations for early detection of breast cancer are highly recommended for women who have the risk factors mentioned above.

Keywords: Risk factors, Probability, Breast cancer

1. INTRODUCTION

WHO reported in 2018 that 2,088,849 new cases of breast cancer every year occurring around the world; thus this become the most common cancer for women and the biggest cause of cancer death among women. This problem still becomes a major health

problem in the world especially in developing countries [1]. Indonesia, as a developing country, breast cancer ranks first for malignancy, which is 65,000 cases or 16.9% of the total 384,809 cancer cases and is the first leading cause of death from malignancy. This number makes Indonesia is becoming the highest country fighting this non-

communicable disease around Southeast Asia (ASEAN) [2]. Jakarta Dharmais Cancer Hospital reported that breast cancer ranked first within the last 10 years until 2018 with a proportion rate of around 40% of the number of other cancer cases [3]. Meanwhile, West Sumatra Province is marked as the third-highest position in the entire country with the prevalence above the national level of 0.9% (2,285 cases) [4]. The data from Dr RSUP. M. Djamil Padang -as well known as the tertiary hospital in West Sumatera shows the increase in the number of outpatient breast cancer, wherein in 2014 as many as 2082 increased to 4132 people in 2018. The increasing incidence of breast cancer is believed to be associated with an increased risk for breast cancer. Each risk of breast cancer in women can have a higher or lower probability, depending on several factors including reproductive factors (age of early menarche, first pregnancy at an advanced age, low parity or childlessness, short or no lactation period have breastfed, endocrine factors (oral contraceptives, hormone replacement therapy), lifestyle factors (obesity, alcohol consumption, smoking, lack of physical activity, and lack of consumption of vegetables/fruit), and genetic factors (family history of breast cancer / ovarian cancer) [5]. Based on the results of a meta-analysis of risk factors for breast cancer in women in Southeast Asian countries, it is known that family history of breast cancer, parity, BMI, age, menopausal status, and use of oral contraceptives are risk factors for breast cancer. [6]. Several other research results related to breast cancer risk factors are known, among others Almeida et al (2015) stated that early menarche, nulliparity, history of breastfeeding less than 12 months / never breast-feeding and lack of physical activity are risk factors for breast cancer in women in Brazil. [7]. Meanwhile, Balekouzou et al (2017) reported that early menarche, giving birth to their first child at an old age (>30 years), parity, and prolonged use of oral contraceptives (>5 years) were risk factors for breast cancer in women in Africa [8]. Aich et al (2016) reported that family history of breast cancer, early menarche, age at first pregnancy, parity, history of breastfeeding, and BMI are risk factors for breast cancer in women in India [9]. A family member of a woman who has cancer has twice the probability of also getting this cancer [10]. The risk factors from ovarian cancer and the younger the age of families suffering from breast cancer are also affected [11]. The use of external estrogen hormones, such as hormone replacement therapy and birth control pills that contain estrogen will increase the risk of breast cancer if used for a long time. because the hormone estrogen plays a role in the emergence of breast cancer [12]. The risk of breast cancer was

also about 20% higher among women who started menstruating before age 11 compared to age 13. The earlier a woman experiences puberty, the higher the risk of developing breast cancer [10]. Women who gave birth to their first child under the age of 30 have a lower risk of developing breast cancer than women who gave birth to their first child after the age of 30 [12]. Breast cancer risk is reduced by 6% for every 12 months of breastfeeding. One possible explanation for this effect is that breastfeeding inhibits menstruation, thereby reducing the number of lifetime menstrual cycles [10]. The more risk factors a woman has, the higher the probability of getting breast cancer. Therefore, it is necessary to further analyze the risk factors for breast cancer in women in West Sumatra. Women who gave birth to their first child under the age of 30 have a lower risk of developing breast cancer than women who gave birth to their first child after the age of 30 [12]. Breast cancer risk is reduced by 6% for every 12 months of breastfeeding. One possible explanation for this effect is that breastfeeding inhibits menstruation, thereby reducing the number of lifetime menstrual cycles [10]. The more risk factors a woman has, the higher the probability of getting breast cancer. Therefore, it is necessary to further analyze the risk factors for breast cancer in women in West Sumatra. Women who gave birth to their first child under the age of 30 have a lower risk of developing breast cancer than women who gave birth to their first child after the age of 30 [12]. Breast cancer risk is reduced by 6% for every 12 months of breastfeeding. One possible explanation for this effect is that breastfeeding inhibits menstruation, thereby reducing the number of lifetime menstrual cycles [10]. The more risk factors a woman has, the higher the probability of getting breast cancer. Therefore, it is necessary to further analyze the risk factors for breast cancer in women in West Sumatra. Breast cancer risk is reduced by 6% for every 12 months of breastfeeding. One possible explanation for this effect is that breastfeeding inhibits menstruation, thereby reducing the number of lifetime menstrual cycles [10]. The more risk factors a woman has, the higher the probability of getting breast cancer. Therefore, it is necessary to further analyze the risk factors for breast cancer in women in West Sumatra. Breast cancer risk is reduced by 6% for every 12 months of breastfeeding. One possible explanation for this effect is that breastfeeding inhibits menstruation, thereby reducing the number of lifetime menstrual cycles [10]. The more risk factors a woman has, the higher the probability of getting breast cancer. Therefore, it is necessary to further analyze the risk factors for breast cancer in women in West Sumatra.

2. METHOD

This research is a quantitative study with a case-control study design through a retrospective approach, with the dependent variable being breast cancer and the independent variables being age, age of menarche, age of menopause, family history, age of the first childbearing, parity, history of breastfeeding, oral contraceptives, therapy hormones, passive smoking, vegetable consumption, fruit consumption, physical activity and BMI (body mass index).

This research was conducted at Dr. RSUP. M. Djamil and Ibn Sina Hospital, Padang City. The sample size is determined by the formula The sample for the paired case-control study design is as follows:

$$P = \frac{OR}{1+OR}$$

$$n = \frac{[Z_{1-\alpha/2} + Z_{F\sqrt{PQ}}]^2}{(P - 1/2)^2}$$

$$n_1 = n_2 = \frac{[1,96 + 0,84\sqrt{0,78 \times 0,22}]^2}{(0,78 - 0,5)^2}$$

$$n_1 = n_2 = 67,94$$

$$n_1 = n_2 = 70$$

Based on the calculation with the formula above, the sample size is 70 people. To anticipate the dropout, a backup sample of 10% (7 people) has been prepared, bringing the total cases to 77 people and being completed to 100 people. So the case samples (women with breast cancer) were 100 people and the control samples (women without breast cancer) were also 100 people (1:1), so the total sample was 200 people. Data were collected using a questionnaire instrument using interviews. Data were analyzed bivariate using chi-square test, and multivariate analysis using logistic regression test. The results of the logistic regression test were also used to estimate the probability of breast cancer in women, by calculating the equation using the following formula:

$$P = \frac{e(B_0 + B_1X_1 + B_2X_2 + B_3X_3 + B_4X_4)}{1 + e(B_0 + B_1X_1 + B_2X_2 + B_3X_3 + B_4X_4)}$$

3. RESULTS AND DISCUSSION

The results of the study can determine the characteristics of the respondents, the relationship of risk factor variables with the incidence of breast cancer (bivariate analysis), the most influential

factors on the incidence of breast cancer (multivariate analysis), and probabilities, as follows:

3.1. Characteristics of Respondents

Characteristics of respondents based on the last education level, it is known that the lowest level is that there are still 2% of respondents who have never attended school in controls, 6% of primary school graduates in cases, and 7% in controls. Employment, more cases did not work (66%) than controls (55%). The more marital status was married and still have a partner in cases (93%) than controls (79%). History of previous cancer was 0% in cases while in controls there were 2% (thyroid cancer and ovarian cancer). There was a history of previous breast disease in 6% of cases, while in controls it was 7% (see table 3.1 for full details).

The level of education will affect the level of knowledge, so it will also affect the attitude and motivation of respondents towards risk factors and efforts to prevent breast cancer. The respondent's work will have implications for information exposure. Respondents who work will find it easier to get information than respondents who do not work. A history of previous breast disease will also affect the incidence of breast cancer.

3.2. Relationship of Risk Factor Variables with Breast Cancer (Bivariate Analysis)

The results of the bivariate analysis revealed a family history of breast cancer, age > 50 years, age at early menarche (<12 years), age at first childbearing >30 years, parity 1/nulliparity, history of breastfeeding, 12 months/never breastfeeding, use of oral contraceptives. >5 years, frequent exposure to cigarette smoke (passive smoking), and lack of fruit consumption were factors that were significantly associated with breast cancer (p<0.05). Meanwhile, late menopause (.55 years), lack of physical activity, lack of vegetable consumption, and excess BMI were not associated with breast cancer because of p-value > 0.05 (see table 3.2 for full details).

The results of this study are similar to those of Balekouzou (2017) that early menarche, giving birth to their first child at an old age (>30 years), parity, and prolonged use of oral contraceptives (>5 years) are risk factors for breast cancer in women in Africa [2]. 8]. This is also in line with research by Hosseinzadeh (2014) that age at menarche, age at first childbearing, parity, history of breastfeeding, and hormone therapy are associated with breast cancer incidence [13]. The results of another study are the same, Sepandi et al (2015) stated that family history of breast cancer, age at first childbearing, parity, history of breastfeeding, passive smoking, and BMI are risk factors for breast cancer in women in Iran [14]. Breast cancer risk can be significantly

Table 3.1 Distribution of Respondents Frequency Based on Characteristics

Characteristics of Respondents	Case		Control	
	F (n=100)	%	f (n=100)	%
Last education				
No school	0	0	2	2
SD	6	6	7	7
junior high school	15	15	25	25
senior High School	46	46	36	36
PT	33	33	30	30
Work				
Work	34	34	46	46
Does not work	66	66	54	54
Marital status				
Not Married	0	0	1	1
Marry	93	93	79	79
Widow	7	7	20	20
Previous history of cancer				
There is	0	0	2	2
There is not any	100	100	98	98
Previous History of Breast Disease				
There is	6	6	7	7
There is not any	94	94	93	93

Table 3.2 Relationship of Risk Factor Variables with Breast Cancer

Variable	Case		Control		P Value	OR (95%CI)
	f (n=100)	%	F (n=100)	%		
Age						
at risk	69	69	54	54	0.029	1.89 (1,064-3,380)
No-Risk	31	31	46	46		
Menarche Age						
at risk	58	58	43	43	0.034	1.83 (1,045-3,207)
No-Risk	42	42	57	57		
Menopause Age						
at risk	14	14	10	10	0.384	1.1 (0.618-3.475)
No-Risk	86	86	90	90		
Family History						
at risk	21	21	5	5	0.001	5.051 (1,821-14,006)
No-Risk	79	79	95	95		
Age of Giving Birth to First Child						
at risk	29	29	6	6	0.001	6.39 (2,521-16,243)
No-Risk	71	71	94	94		
parity						
at risk	32	32	18	18	0.022	2.14 (1.107-4.152)
No-Risk	68	68	82	82		
Breastfeeding History						
at risk	34	34	11	11	0.001	4.16 (1,967-8.830)
No-Risk	66	66	89	89		
Oral Contraception						
at risk	36	36	23	23	0.044	1.88 (1.014-3.498)
No-Risk	64	64	77	77		
Hormone Therapy						
at risk	0	0	0	0	Cannot do a statistical test	

No-Risk	100	100	100	100		
Smoke						2.27
at risk	86	86	73	73	0.023	(1.109-
No-Risk	14	14	27	27		4.653)
Physical Activity (Sports)						
Not enough	94	94	93	93		
Enough	6	6	7	7	0.774	1.1
						(0.382-
						3.641)
Vegetable Consumption						1.1
Not enough	46	46	42	42	0.569	(0.673-
Enough	54	54	58	58		2.057)
Fruit Consumption						2.00
Not enough	81	81	68	68	0.035	(1.044-
Enough	19	19	32	32		3.854)
BMI						0.8
at risk	46	46	51	51	0.479	(0.470-
No-Risk	54	54	49	49		1.426)

Table 3.3 Results of Preliminary Modeling of Multivariate Analysis (The most significant variable affects the incidence of breast cancer)

Variable	Model 0 p nilai value	Model 1 p nilai value	Model 2 p nilai value	Model 3 p nilai value	Model 4 p nilai value
Age	0.029	0.033	0.032	0.026	0.031
Age of menarche	0.034	0.163	0.150	0.136	-
Family history/ Genetics	0.001	0.008	0.007	0.005	0.004
Age of first birth	0.001	0.002	0.001	0.001	0.001
Breastfeeding history	0.001	0.009	0.008	0.008	0.005
parity	0.022	0.067	0.066	0.064	0.059
Use of Oral Contraceptives	0.044	0.493	-	-	-
Smoking/Exposure to Cigarette Smoke	0.023	0.230	0.206	-	-
Fruit Consumption	0.035	0.087	0.063	0.068	0.084

Table 3.4 Final Modeling Results of Multivariate Analysis

Variable	B	P	Exp (B)	CI (95%)
Age	0.752	0.024	2.12	1.10 – 4.07
Family history	1.485	0.007	4.41	1.49 – 13.04
Age of giving birth to first child	1,818	0.001	6.16	2.33 – 16.28
Breastfeeding history	1,270	0.002	3.56	1.59 – 7.97

increased for women with first-degree relatives (mother, sister, or daughter) with breast cancer. The risk can be doubled if there is more than one nuclear family member affected by breast cancer and the younger the family member with breast cancer, the greater the disease is hereditary [5]. The older you have your first child, the greater the risk for breast

cancer, this is because the period between the age of menarche and the first gestational age occurs when there is a hormonal imbalance and breast tissue is very sensitive to it, so this period is the beginning of the development of breast cancer [15]. Besides, women who breastfeed their children, especially for more than a year, are at a lower risk of developing

breast cancer. During breastfeeding, breast cells become more mature (mature). By breastfeeding a person's menstruation will be delayed thereby reducing the menstrual cycle, this reduces the body's exposure to the hormone estrogen, thereby reducing the risk of breast cancer [12]. Nulliparity (not having children) or having only one child (parity one) can increase the risk of breast cancer due to longer exposure to the hormone estrogen. High levels of the hormone estrogen during a woman's reproductive years, especially if not accompanied by hormonal changes in pregnancy, increase the chances of growth of cells that are genetically damaged and cause cancer [16]. Oral contraceptives are contraceptives that contain the hormone estrogen. The hormone estrogen is associated with the occurrence of breast cancer. Women who are exposed to this hormone for a long time have a high risk of developing breast cancer, so long-term use of oral contraceptives is a risk factor for breast cancer [10]. Women who smoke passively are at risk for breast cancer because exposure to cigarette smoke has a strong relationship with DNA damage triggered by oxidative stress and carcinogenesis [10]. The probability of a woman getting breast cancer will be higher along with the more risk factors she has [11]. An increase in a woman's age goes hand in hand with an increased risk for breast cancer. The risk of developing breast cancer is 2-4 times greater in women who experience menarche before the age of 12 years. Where, women who experience menarche before the age of 12 years (early menarche) will result in higher estrogen exposure, which is known to increase the risk of breast cancer. The risk of breast cancer decreases by about 10% for every 2 years of delay in the age of the first menstruation. Early menstruation is closely related to increased levels of estradiol which can later continue until a woman grows up. High levels of the hormone estradiol trigger a person to get breast cancer [13]. Lack of fruit consumption in daily life increases the risk of breast cancer [17]. Fruit contains vitamin C, vitamin E, and selenium which function as anti-carcinogenic substances,

3.3. The Most Influential Risk Factors for Breast Cancer Incidence (Multivariate Analysis).

The results of multivariate analysis showed that age, family history of breast cancer, age of giving birth to their first child, and history of breastfeeding had a significant effect on breast cancer (p -value <0.05). The most dominant factor influencing breast cancer was the age of giving birth to the first child

($p = 0.001$, $\text{Exp (B)} = 6.16$, $95\% \text{ CI} = 2.33\text{--}16.28$, $B \text{ value} = 1.818$). table 3.4).

3.4. Probability of a woman getting breast cancer

Based on the results of logistic regression tests and calculations using the equation formula, it is known that the probability of a woman getting breast cancer is 76.46% if she has 4 risk factors from the results of multivariate analysis, namely age > 50 years, there is a family history of breast cancer, age at giving birth to her first child > 30 years and history of breastfeeding <12 months / never breastfed.

4. CONCLUSIONS AND SUGGESTIONS

This study shows that the risk factors for breast cancer among women in West Sumatra are related to genetic factors, reproductive factors, and lifestyle. Therefore, it is necessary to provide health education about risk factors for breast cancer, and periodic examinations for early detection of breast cancer are highly recommended for women who have risk factors.

AUTHOR'S CONTRIBUTION

The author's contributions in this study include preliminary surveys, making proposals, managing permits, collecting data, processing and analyzing data, making reports, and making manuscripts for publication.

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