

The Effect of Abortion, Use of Hormonal Contraception, First Age of Pregnancy and Parity on the Incidence of Breast Cancer at the Riau Referral Hospital

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ABSTRACT

Background: Breast cancer is a cancer in women with a high percentage of 34% of all cancers and 12.8% of sufferers causing death. It is estimated that breast cancer will reach 3.2 million by 2050. In 2018, 365 out of 580 cases of cancer treated were breast cancer. There was an increase in outpatient visits at the oncology polyclinic in 2016 - 2018 from 1286 to 2495

Objective: This study aims to determine the level of correlation between, history of abortion, use of hormonal contraception, age at first birth and parity with the incidence of breast cancer.

Methods: This research is quantitative analytic observational with a case control design by taking medical register data and interviews from research respondents. This research was conducted at ArifinAchmad Referral Hospital, Riau Province on July 2-12, 2019. There were 324 new patients and old patients with Anatomical Pathology (PA) results of breast tissue as breast cancer.

Result: The results of the omnibus test of model coefficient = 0.000 ., Nagelkerke R Square value = 0.242, which means that there is a significant relationship between abortion history, history of use of hormonal contraceptives, age at first birth and parity with the incidence of breast cancer 24.2%. $p = 0.035$, history of using hormonal contraceptives ($p = 0.00$), age at first birth ($p = 0.01$), number of children ($p = 0.042$)

Discussion: From the multivariate analysis, it was found that there was an increase in the incidence of breast cancer in women with: history of abortion was 3.7 times; a history of using hormonal contraception 5.4 times; age of giving birth to their first child over 35 years is 3.0 times, while nulliparous women have 2.3 times the risk

Keywords:

breast cancer, abortion, hormonal contraception, age at first delivery, parity

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1. Background

Breast cancer is the biggest problem for women in all over the world, including Indonesia, with an incidence of 38 per 100,000 women¹. It is estimated that around 18.1 million new cancer cases and 9.6 million deaths from cancer in 2018. Deaths from female breast cancer are approximately (11.6%)²

Breast cancer is the most commonly diagnosed cancer and the second leading cause of cancer death, after lung cancer. In 2012, 1.67 million new cases of breast cancer were identified worldwide, accounting for 25% of all cancers. In the same year an estimated 226,870 new cases of invasive breast cancer and 39,510 deaths due to breast cancer occurred among US women³. In 2017 the estimated new cases of invasive breast cancer were 252,710 cases and 40,610 deaths were estimated. women in the US are at risk for breast cancer and one in thirty five (1:35) sufferers die from breast cancer. Breast cancer incidence rates vary in different parts of the world, from 27 per 100,000 in Central Africa, East Asia and 92 per 100,000 in North America. The world breast cancer incidence rate is estimated to reach 3.2 million by 2050.⁴ Breast cancer mortality is higher in less developed areas. Breast cancer deaths are higher in less developed areas.

Based on Basic Health Research Data in 2013, the number of breast cancer patients reached 61,682 cases in Indonesia⁵. The Indonesian Ministry of Health in 2015 stated that breast cancer is a cancer with the highest percentage of new cases, namely 43.3% and the percentage of cancer deaths. breast cancer is 12.8%⁶. While the 2010 National Cancer Registry reports for the Polish population that there were 15,784 new breast cancer cases, or 22% of all cancers, and 80% occurred at age 50 and over, 50% were aged 50 - 69 years, and more than 5000 women died. According to the medical records of the ArifinAchmad Referral Hospital in Riau Province, breast cancer ranks first with 325 cases out of 580 cases treated in 2016. The number of visits to breast cancer patients in 2016 was 1286 visits and increased to 2511 in 2017 slightly decreased to 2495 in 2018.

Many intrinsic and extrinsic factors influence the occurrence of breast cancer, such as age, history of abortion, heredity, age at first menstruation and history of cancer or genetics, marital status, age at first birth, number of children, history of use of hormonal contraceptives for birth control, duration of use birth control hormonal contraceptives, history of breastfeeding, duration of breastfeeding, food consumption patterns and physical activity⁷. The first delivery is over 35 years old, gets estrogen and progesterone hormones as hormone replacement therapy (HRT) in menopause, menstruation at less than 12 years of age, menopause After 55 years of age, receiving oral contraceptives for more than 10 years, not breastfeeding, overweight, especially at menopause, the risk increases by 30% to 60%. Oral contraceptive pill (OC) therapy in menopausal women has a low risk of breast cancer OR 1.24 (1.0-1.53)⁸.

Multiparous women have a lower risk of developing breast cancer because Estrogen Receptor (ER) is lower than nulliparous, OR = 0.82 [0.77-0.88] especially multiparous breastfeeding is lower than women who never breastfeed 0.82 [0.74-0.91])⁹. Multiparous women with ≥ 3 children who are breastfeeding have an incidence of 0.78 [0.62-0.98] times; whereas never breastfeeding was, 0.76 [0.58-1.00])⁹. The risk of basal-like breast cancer was higher among women with higher parity who had never breastfed. Women who have never given birth have a higher risk of breast cancer than women who are multiparous

According to David J Hunter, from 1344 cases (n = 116,606) diagnosed with breast cancer using Oral Contraception (OC) in women between the ages of 25-42 years, it was concluded that OC use had a greater risk of developing breast cancer. The use of levonorgestrel in triphasic preparations caused an increased relative risk with an OR of 1.12; 95% confidence interval 0.95-1.33]¹⁰. While Elizabeth B in a cross-sectional study of 1,102 women between the ages of 20 and 39 who used OC, there was an increase in the incidence of breast cancer¹¹.

Women with a history of abortion are 6 times more likely to suffer from breast cancer because of exposure to high concentrations of estrogen so that the cells are not properly differentiated. There is an association between women with a history of spontaneous abortion and breast cancer¹².

According to Jiang, Ai-Ren does have a relative relationship between abortion and breast cancer. The combination of spontaneous abortion and a positive ER negative ER genotype can be a marker of breast cancer susceptibility¹³. In premenopausal women who experience abortion, the incidence of breast cancer is 3 times higher, whereas in postmenopausal women who have repeated abortions the incidence of breast cancer is 2 times. analysis of many prospective cohort studies worldwide.¹⁵ However, it was later stated that abortion is a risk factor for breast cancer

Women who give birth to their first child at an advanced age have a higher risk of breast cancer than women who have their first child at a younger age, and about 40% more women who have their first child after age 35 are at risk of developing breast cancer than women who had their first child before the age of 20 years¹⁶. Women who gave birth after 25 years of age have been reported to be associated with an increased risk of ER-PR negative cancer by 2 times. However,

when accompanied by breastfeeding, the risk of breast cancer is small.¹⁷ Women over 35 years of age who give birth to their first child have a lower risk of developing breast cancer compared to those who have never given birth¹⁶. This means that breastfeeding can reduce the incidence of breast cancer. During pregnancy, breast cells grow rapidly, if there is genetic damage to breast cells before pregnancy, and genetic damage continues to increase in the cells, this can lead to breast cancer. The likelihood of genetic defects increases with age. This could help explain why women who had their first child at an older age had a higher risk of breast cancer than women who had their first child at a younger age. However, women over the age of 35 who gave birth only once had a slightly higher risk of breast cancer compared to women who never gave birth¹⁸. In general, the more often a woman gives birth, the lower her risk of developing breast cancer. After the first child, each subsequent delivery lowers the risk. Some findings suggest childbirth only lowers the risk of estrogen receptor positive, with no effect on the risk of estrogen receptor-negative breast cancer. Birth spacing plays a role in the incidence of breast cancer, delivery at large intervals increases the incidence of cancer¹⁹, this may be related to changes in breast cells that occur during pregnancy²⁰. The increased interval between first birth and 5 years was associated with an increased risk of lobular breast cancer. In contrast to ductal cancer, premenopausal women with a shorter time interval (less than 2 years) between the first and second births had a greater risk than the longer interval (more than 3 years) was associated with a reduced risk. Meanwhile, the distance between the 2nd and 5th births does not affect the risk of ductal breast cancer²⁰.

Based on the data above, the researchers wanted to find out whether there was a relationship between history of abortion, use of hormonal contraception, age at first birth and parity with the incidence of breast cancer at ArifinAchmad Referral Hospital Pekanbaru, Riau, Indonesia.

2. Methods

This research is a quantitative analytic observational study with a case control design by taking medical register data and interviews from research respondents. This research was conducted at the ArifinAchmad Referral Hospital in Riau Province from 2 July to 12 July 2019, on 324 new and old cases with positive breast cancer Anatomical Pathology (PA) results. Meanwhile, control patients were patients whose anatomical pathology diagnosis was negative for breast cancer. Determination of the number of samples in this study using the minimum number of samples for each variable, namely 15 samples. So that the number of samples of cases and controls becomes 240 people. Inclusion criteria Already married and willing to be respondents. While the exclusion criteria: the subject was sick when interviewed and the subject had 1 child. Sampling by consecutive sampling through medical record data from the Laboratory of Pathology Anatomy (PA) ArifinAchmad Hospital, then an interview was carried out according to a questionnaire by telephone. Data analysis was performed using univariate, bivariate and multivariate methods. Ethics of Health Research at the Hangtuah College of Health Sciences Pekanbaru number: 187 / KEPK / STIKes-HTP / IV / 2019

3. Result

Table 1. The Relationship of Independent Variables to Cancer Incidence

No	Test variable	Breast Cancer Incidence						P value	OR 95% CI
		Case		Control		Total			
		n	%	N	%	n	%		
1	Age								
	> 50 years old	54	45.0	55	45.8	109	45.4	1,000	
	<50 years old	66	55.0	65	54.2	131	54.6		
	total	120	100	120	100	240	100		
2	Abortion history								
	Ever	18	15.0	7	5.8	25	10.4	0.0 35 2,849 (1,143 - 7,100)	
	Never	102	85.0	113	94.2	215	89.6		
	total	120	100	120	100	240	100		
3	History of contraceptive use								
	Ever	38	31.7	9	7.5	47	19.6	0.0 01 5,715 (2,618 - 12,476)	
	Never	82	68.3	111	92.5	193	80.4		
	total	120	100	120	100	240	100		
4	Long use of hormonal contraception								
	> 5 years	16	13.3	6	5.0	22	9.2	0.044 2,923 (1,102-7,751)	
	≤5 years	104	86.7	114	95.0	218	90.8		
	total	120	100	120	100	240	100		
5	History of breastfeeding								
	Do not do	51	42.5	35	29.2	86	35.8	0, 043 1,795 (1,052 - 3,064)	
	To do	69	57.5	85	70.8	154	64.2		
	total	120	100	120	100	240	100		
6	Long time giving breast milk								
	<1 year	41	34.2	26	21.7	67	27.9	0.044 1,876 (1,056-3,335)	
	≥1 years	79	65.8	94	78.3	173	72.1		
	total	120	100	120	100	240	100		
7	Age of giving birth to first child								
	> 35 years old	49	40.8	21	17.5	70	29.2	0, 001 3,254 (1,794 - 5,900)	
	≤35 years old	71	59.2	99	82.5	170	70.8		
	total	120	100	120	100	240	100		

8 parity							
Nulipara	40	33.3	25	20.8	65	27.1	
Multipara	80	66.7	95	79.2	175	72.9	0.042
total	120	100	120	100	240	100	1,900 (1,062-3,399)

The multivariate analysis used in this study is multiple logistic regression test which aims to determine the relationship between the most dominant independent variable and the dependent variable.

No	Variable	P value	OR	95% CI	
				Lower	Upper
1	Abortion history	0.008	3,765	1,414	10,025
2	History of hormonal contraceptive use	0.001	5,407	2,391	12,225
3	Age of childbirth	0.001	3,091	1,620	5,895
4	Parity	0.010	2,338	1,228	4,452

1) The results of the omnibus test of model coefficient = 0.000, which means that the resulting model is suitable for use. Nagelkerke R Square value = 0.242, meaning that the independent variable is history of abortion, history of using hormonal contraceptives, age at first birth and number of children can explain the variable incidence of breast cancer 24.2%,

2) Respondents with a history of abortion had a 3.7 times greater risk of developing breast cancer than respondents who had no history of abortion (OR = 3.765, 95% CI = 1.414-10.025)

3) Respondents who had a history of using hormonal contraceptives had a 5.4 times greater risk of breast cancer than respondents who had no history of using hormonal contraceptives (OR = 5.407, 95% CI = 2,391-12,225)

4) Respondents with age at giving birth to their first child > 35 years had a 3 times greater risk of developing breast cancer than respondents with age at birth for their first child ≤ 35 years (OR = 3.091, 95% CI = 1.620-5.895)

5) Respondents with nulliparous children were 2.3 times more likely to have breast cancer than respondents with multiparous children (OR = 2.338, 95% CI = 1.228-4.452)

4. Discussion

1. History of Abortion

From the results of the research conducted, it was found that there was a significant relationship between abortion history and the incidence of breast cancer in women with a p value of 0.008 (OR = 3.765 95% CI = 1.414-10.025). Bhadoria (2013) states that women with a history of abortion are 6 times more likely to suffer from breast cancer¹². This is due to the inhibition of the natural maturation process of the breast, thereby increasing the risk of breast cancer. During pregnancy until gestational age <32 weeks the breasts undergo tissue changes, which are susceptible to carcinogens²¹. A population-based case-control study with 669 cases and 682 controls in Jiangsu Province China. Induced abortion is associated with an increased risk of breast cancer. Premenopausal women who underwent ≥ 3 times induction of abortion obtained OR (2.41, 95% CI: 1.09-5.42) and became OR (1.55, 95% CI: 1.15-5.68). Meanwhile,

postmenopausal women with previous induced abortion OR (2.04, 95% CI: 1.48-2.81) and became OR (1.82, 95% CI: 1.30-2.54), and there was a tendency significant increase in OR by number of induced abortions (p for trend: 0.0001)¹⁴. Induction of abortion significantly increased the risk of breast cancer among Chinese women 1.76 (95% CI 1.39-2.22), and the risk of breast cancer increased with the increase in the number of induced abortions 1.89 (95% CI 1.40- 2.55)²². However Since 2003, ACOG and the National Cancer Institute (NCI) have agreed scientific evidence does not support a link between abortion and breast cancer²³.

2. History of Use of Hormonal Contraceptives

There is a significant relationship between the history of using hormonal contraceptives with the incidence of breast cancer with p value = 0.001 (OR = 5.407 95% CI = 2.391-12.225). it means that there is a risk of 5.4 times the incidence of breast cancer compared to respondents who do not use hormonal contraceptives.²⁴ Prasetyowati found that the incidence of breast cancer in women with a history of hormonal contraceptive use was 3.3 times more at risk than those without a history of using hormonal contraceptives²⁵. Users of contraceptive pills (OC) and injections for a long period of time trigger cancer²⁶. Harianto said users Combined contraceptive pills have a risk 1,864 times greater than those who do not use the contraceptive pill²⁷. From the meta-analysis results of OC therapy in menopausal women have a low risk for breast cancer OR 1.24 (1.0-1.53) in those containing estrogen-progesterone, whereas which is only estrogen 0.79 (0.6-1.02)²⁸. Elizabeth B in a cross-sectional study of 1,102 women between the ages of 20 and 39 who used OC there was an increased incidence of breast cancer including: high doses of estrogen (OR, 2.7 (1.1–6.2), ethynodioldiacetate (OR, 2.6 (1.4–4.7) , or triphasic at a dose of 0.75 mg norethindrone OR, 3.1 (1.9–5.1)¹¹. David J Hunter's study, of 1344 cases (n = 116,606) diagnosed with breast cancer using OC in women between the ages of 25-42 years, the relative risk of breast cancer was OR 1.12 (0.95-1.33) .High risk 1.33 (1.03-1.73) . Triphasic preparations with levonorgestrel as progestin OR 3.05 (2.00-4.66)¹⁰.

3. The age at which the first child was born

There is a significant relationship between the age of giving birth to the first child > 35 years with the incidence of breast cancer p value 0.001 (OR = 3.091 95% CI = 1.620-5.895), compared to giving birth to the first child <35 years. According to Sarah Lord, women who first gave birth after age 25, having had a previous pregnancy were associated with an increased risk of estrogen receptor (ER) progesterone receptor (PR) negative cancer (OR = 2.07, 95% CI = 1.03-4 , 16)¹⁷. However, when accompanied by breastfeeding, the risk of breast cancer is small. Nani D at Pertamina Hospital Cilacap, who stated that there was a relationship between gestational age > 35 years with the influence of cell abnormalities in the breast, the level of estrogen exposure in him was getting higher⁸. First births aged <20 years and > 35 years had 6 times the risk of experiencing breast cancer while Nulipara had a 4.3 times higher risk of developing breast cancer than multiparous according to^{29,30}.

4. Parity

There was a significant relationship between the number of children and the incidence of breast cancer in nulliparous women with a p value of 0.010 (OR = 2.338 95% CI = 1.228-4.452) compared to multiparous. Concerned stated that there was a relationship between the number of

children and the incidence of breast cancer³⁰. Meanwhile, Ardiana stated that the parity factor had a significant relationship with the incidence of breast cancer with OR = 6.38³¹.

Increased parity, high circulating hormone levels during pregnancy lead to differentiation of The Terminal Duct-Lobular Unit (TDLU), which is protective against permanent breast cancer growth and nulliparous women have a 30% risk of developing cancer compared with multiparous women.³² Multiparous women have a lower risk of developing estrogen receptor (ER) breast cancer than nulliparous, hormone receptor (HR) = 0.82 [0.77-0.88]. nulliparous women had a higher incidence than multiparous women of B-luminal breast cancer regardless of breastfeeding (≥ 3 children: breastfed, 0.78 [0.62-0.98]; never breastfed, 0.76 [0.58-1, 00])⁹.

5. Conclusion

1. Women with a history of abortion have a 3.7 times greater risk of developing breast cancer than those without a history of abortion
2. Women who have a history of using hormonal contraceptives are at an increased risk of 5.4 times the risk of breast cancer than those who do not have a history of using hormonal contraceptives
3. Women with the age of giving birth to their first child > 35 years are three times more likely to have a risk of breast cancer than those with age at birth for their first child ≤ 35 years
4. nulliparous women were 2.3 times more likely to have breast cancer than the number of multiparous children

The limitations of the study are the number of samples and the limited time of the study, so that more samples are needed and other additional variables are needed

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