Risk Factors of Breast Cancer in Patients at Dr. Doris Sylvanus Hospital, Palangka Raya

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Abstract: Breast cancer ranks first in contributes to cancer deaths in Indonesia. This study aims to analyze the relationship between menarche age, level of knowledge, and history of the use of control birth pills and the incidence of breast cancer. This study employed a case-control design. Inclusion criteria for the case group were women, 20–50 years, breast cancer patients, junior high education level, and married. The subjects excluded respondents who used contraception. The data comes from questioner and medical record. There were 27 respondents each for the case and control group. The result showed a major age range of 31–40 years (63.0%). The education level was dominated by junior high school (40.7%). The chi-square test showed a correlation between the age of menarche (p = 0.01) OR 5.50 (95% CI: 1.604 -18.864), and knowledge (p = 0.00) OR value of 8.31 (95% CI: 2.437-28.354) with breast cancer, but no correlation between history of use of pills contraception with breast cancer (p = 0.74). The dominant risk factor for breast cancer in patients at Dr. Doris Sylvanus Hospital was the level of knowledge. Increasing knowledge about cancer is important in preventing breast cancer in women, especially in Palangkaraya.

Keywords: breast cancer; age of menarche; contraception pills; level of knowledge

INTRODUCTION

Breast cancer currently ranks first with the largest number of cancers in Indonesia (16.6%) out of a total of 396.914 cases for all types of cancer. Breast cancer is also one of the first contributors to cancer deaths. According to prevalence data from Globocan 2020, the number of deaths from breast cancer reached more than 22 thousand. Furthermore, the number of new cases of breast cancer among women in 2020 reached 65.858 (30.8%) of a total of 213.546 new cases in Indonesia.[1]

An early cancer detection program in the city of Palangka Raya, Kalimantan Tengah, has been implemented since 2015 with the priority of detecting the most important cancers of the uterus and breast cancer. In 2015–2018 in Central Kalimantan, women aged 30–50 who performed early detection of breast cancer through the SADANIS examination method were screened positive for breast cancer by 5,07%. Breast Cancer Screening with the Clinical Breast Examination (CBE) Method in women aged 30–50 years in 2017 found as many as 1 case (0.10%) of the total examination of 899. In 2018, there were 8 cases (2%) of tumor or tumor discovery out of a total of 444 women aged 30–50 the year. In 2019, there was an increase in 36 cases (5%) of tumors out of a total of 646 people examined.[2]

Dr. Doris Sylvanus Hospital is the largest reference hospital in Central Kalimantan Province. Patient data on road care with a diagnosis of malignant breast neoplasm in 2019 amounted to 2,100 cases. For the data on street care patients with diagnoses of malignant breast neoplasms in 2020, there were 1,988 cases. Patient data on road care with diagnoses of malignant breast neoplasms in 2021 amounted to 2,821 cases. Data from 2019 to 2021 tended to increase.[3]

One of the risk factors for breast cancer is the age of menarche. If a woman has menstruation at an early age (before 12 years), she will have an increased risk of breast cancer because the sooner she

experiences puberty is, the longer the breast tissue is exposed to harmful elements that cause cancer, such as chemicals, estrogen, or radiation that affect the process of tissue proliferation, including breast tissues. Early menarche will also cause multiple menstrual cycles and repeated increases in estrogen and have a stimulating effect on the mammalian epithelium, thus increasing the likelihood of abnormalities in breast tissue. The mechanism of breast cancer caused by exposure to estrogen is caused by the stimulation of estrogen itself against the division of epithelial cells or by estrogen and its metabolites directly acting as mutagens. This hormone begins to be active when women first experience menstruation or menarche. Hormone levels of estrogen and early menarche can be affected by several aspects, including lifestyle factors such as high-fat foods, low fiber, excess weight, and less physical activity.[4,5]

Another risk factor is that using hormonal contraceptives for >5 years can increase the risk of breast cancer by 1.52 times. It can occur due to the accumulation of the hormone estrogen in the body. This accumulation of estrogen can also lead to obesity due to increased levels of fat in the body. There was a 24% increase in breast cancer risk among oral contraceptive users. Users of oral contraceptives with high doses of estrogen can increase their risk of breast cancer by 10–30%. The mechanism by which the hormone estrogen stimulates the growth of the ductus in the breast glands longer charging of the hormone estrogen can cause changes in the ductus cells in the breast glands. These changes can cause abnormal hypertrophy and proliferation that can eventually turn into cancer.[6-8]

There is also an external risk factor for breast cancer. Knowledge is the domain that forms a person's actions from experience; behavior based on knowledge will be more lasting than behavior that is not based on knowledge. Notoadmojo (2013) explains that knowledge, attitudes, beliefs, and traditions determine the behavior of a person or society about health. There is still a lack of awareness among Indonesian women about early detection of breast cancer because there are still many who do not know how to detect early breast cancer, which causes the incidence of breast cancer to be quite high. The provision and reception of good information about SADARI examination and knowledge related to breast cancer can contribute directly to the improvement of knowledge about breast cancer and affect early detection behavior and efforts to conduct early examinations at the health care center for symptoms perceived in the breast.[9,10]

Previous studies have found different results. Studies conducted by Purwanti, Syukur, and Haloho (2021) and the results of the Ningrum and Rahayu study (2021) showed that there is a significant relationship between menarche age and breast cancer incidence in women. However, the studies by Maysarah and Dede (2016) and the Hutasoit study (2017) revealed that there was no link between menarche age and breast cancer incidence in women.[11-14]

The previous studies by Fatmawati (2020) and Prabandari and Fajarsari (2017) found that there was a significant relationship between the history of hormonal contraception use and breast cancer. The results differ from the study of Mariahadi (2017) and Madjid et al, (2022), which stated that there was no significant relationship between the history of hormonal CB use and the incidence of breast cancer. [15-18]

The results of Tambunan's (2017) and Sari's (2017) research showed that there is a link between the level of knowledge and early detection of breast cancer. However, unlike the results of Immawati and Utami (2017) and Toki and Kelen (2019) studies, there is no significant relationship between the level of knowledge and early detection of breast cancer.[19-22]

Based on the global phenomenon of breast cancer, as well as the results of preliminary studies, it is important to conduct studies on breast cancer risk factors in women to prevent and treat breast cancer properly and effectively.

MATERIAL AND METHOD

The research ethics have gone through an ethical test from the Health Ethics Commission of Medical Faculty of Universitas Lambung Mangkurat, issued with number 030/KEPK-FK ULM/EC/III/2023 so that the research is worthy of being carried out carefully. This research is an observational analytical study with the design of a case-control study, where the case group is women with breast cancer and the control group is women who do not have breast cancer. The study was conducted at Dr. Doris Sylvanus Hospital Palangka Raya. The population in this study is all female patients; as many as 250 people were counted during the collection of research data from February to May 2023.

The method of sampling used is consecutive sampling, i.e., all subjects that come in and meet the selection criteria are included in the study until the required number of subjects is met. The large sample size of the study was determined based on the Lemeshow formula, obtaining the results of 24 people for the

control group and 24 people for the case group. To anticipate the dropout, plus 10% of the sample, 27 people were obtained for the control group, and 27 people for the case group.[23]

The inclusion criteria for the subjects of the case study group are women aged 20–50 years, breast cancer patients, minimum education of secondary school, married, has already experienced menstruation, and willing to be respondent. The diagnosis of breast cancer based on the results of a biopsy and positive histopathology examination stated in the medical records. The inclusion criteria of the subjects of control group are women aged 20–50 years, not suffering from cancer, no family bond with breast cancer in the case group, minimum education of secondary school, married, has already experienced menstruation, and willing to be respondent. The exclusion criteria for the subjects of this study are female patients who were seriously ill and not to be able to fill out the questionnaire or refused to fill it out, women who used contraception injections, contraception implants, and intra unterine device/IUD.

This research instrument was a level-of-knowledge. The questionnaire was declared valid and reliable with a validity test result of r counting > 0.3 on 20 statements, and the reliability test Cronbach's Alpha value was 0.83 (> 0.6). The collection of research data was carried out through the following stages: determining the criteria of inclusion and exclusion of research respondents, performs the verification data of cases group (pregnant breast cancer) and control group by checking the medical records, and filling out a questionnaire by respondents. Data correlation between the age of menarche with breast cancer, knowledge level with breast cancer, and history of use of pills contraception with breast cancer was analyzed using the chi-square test.

RESULT

Data on the number of breast cancer cases was quite high and has increased in the last 3 years in Dr. Doris Sylvanus Hospital Palangka Raya: 2,100 cases in 2019, 1,988 cases in 2020, and 2,821 cases in 2021. This study aims to analyze the relationship between the history of the use of contraception pills, the history of menarche age, and the level of knowledge with the occurrence of breast cancer.

Table 1. Characteristics of Research Subject

Characteristic of Subject	Frequency	Percentage
Age of respondent		
20-30 years	12	22.2 %
31-40 years	34	63.0 %
41-50 years	8	14.8 %
Level of education		
Junior High School	22	40.7 %
High School	20	37.0 %
Bachelor Degree	12	22.2 %
Menarche age		
< 12 years	20	37.0 %
≥ 12 years	34	63.0 %
Pills contraception use		
≥ 5 years	12	22.2 %
< 5 years	42	77.8 %
Level of knowledge		
Bad	25	46.3 %
Good	29	53.7 %

Based on Table 1, the majority of respondents were in the age range of 31-40 years (63.0%). The educational level of respondents is dominated by Junior High School (40.7%). The menarche age of respondents was predominantly in the age range of ≥ 12 years (63.0%). The history of contraception pill use was predominant among respondents with the use of < 5 years (77.8%). The level of knowledge of respondents was dominated by good knowledge (53.7%).

Table 2. Relationship between menarche age and breast cancer

Variable menarche age	Breast cancer						OR (95 % CI)	P value
	Case		Control		Number Of			
	n	%	n	%	n	%		
< 12 years	15	55.6 %	5	18.5 %	20	37.0 %	5.50 (1.604-18.864)	0.001
≥ 12 years	12	44.4 %	22	81.5 %	34	63.0 %		
Total	27	100%	27	100 %	54	100 %		

Based on Table 2, the results of the case group revealed more respondents with an age of < 12 years, 15 people (55.6%) compared to the control group of 5 people (18.5%). Then, the p = 0.01 (p ≤ 0.05) result was obtained, indicating a relationship between menarche age and breast cancer and an OR value of 5.50 (95% CI: 1.604 -18.864). It means that respondents who are under 12 years of age were 5.50 times more likely to develop breast cancer compared to respondents whose age is ≥ 12 years.

Table 3. The relationship between the history of the use of contraceltion pills with breast cancer

Variable History of contraception pills	Breast Cancer						P value
	Case		Control		Total		
	n	%	n	%	n	%	
≥ 5 years	5	18.5 %	7	25.9 %	12	22.2 %	0.74
< 5 years	22	81.5 %	20	74.1 %	42	77.8 %	
Total	27	100%	27	100 %	54	100 %	

Based on Table 3, the results of the case group revealed more respondents who took contraception pills for < 5 years, 22 people (81.5%), compared to the control group, the respondents with more respondents using contraception pills < 5 years of 20 people (74.1%). There was no association between the history of contraception pill use and the incidence of breast cancer p 0.74 (p ≥0.05)

Table 4. Relationship between knowledge levels with breast cancer

Level of knowledge variable	Breast Cancer						OR (95 % CI)	P value
	Case	Control			Total			
	N	%	n	%	n	%		
Bad	19	70.4 %	6	22.2 %	25	43.3 %	8.31 (2.437-28.354)	0.00
Good	8	29.6 %	21	77.8 %	29	53.7 %		
Total	27	100%	27	100 %	54	100 %		

Based on Table 4, the results of the case group were more respondents with a poor level of knowledge, 19 people (70.4%), compared to the control group of 6 people (22.2%). Then the p 0.00 value was obtained, indicating a relationship between the level of knowledge with the incidence of breast cancer and the OR value of 8.31 (95% CI: 2.437-28.354). It means respondents with poor knowledge were 8.31 times more likely to develop breast cancer compared to respondents who had good knowledge.

Table 5. Multivariate analysis Selection of free variables that meet the criteria of the multivariate model

No	Independent Variable	P value	Identifying
1	Use of contraception pills	0.743	Not included
2	Menarche Age	0.015	Included
3	Level of knowledge	0.001	Included

Based on Table 5, free variables included in the multivariate model are menarche age variables and level of knowledge as the variable has a p-value < 0.25. Meanwhile, the variable history of the use of tablets contraception is not included as the p value > 0.25 is 0.74.

Tabel 6. Analysis of Multi-variant regression model of logistics

No	Free Variable	B	Sig.	Exp (B)	95 % CI
1	Menarche Age	1.631	0.021	5.107	0.704-5.368
2	Level of knowledge	2.062	0.002	7.859	0.668

According to Table 6, the age variable menarche has a significance value of 0.021, indicating a significant relationship between the age variant menarche and breast cancer. Furthermore, the significance

value of the knowledge-level variable is 0.002, indicating a significant relationship between the knowledge-level variable and breast cancer. Then, the most dominant variable that influenced the incidence of breast cancer is the knowledge level variable with an Exp(B) value of 7.859.

DISCUSSION

Relationship between menarche and breast cancer

The case group was dominated by respondents with a history of menarche aged <12 years (55.6%) when compared to the control group with menarche age < 12 years, which was 5 people (18.5%). The results of this study showed a meaningful relationship between menarche age and breast cancer incidence. Women who are under the age of 12 have a 5.50 times higher risk of developing breast cancer than women who are older than 12 years of age. It can be explained that the group of women who have their first menstrual period under the age of 12 have a higher risk of developing breast cancer; this condition is associated with longer estrogen exposure times, leading to the greater risk of becoming cancer cells. The hormone estrogen in women is associated with the development of breast cancer. The mechanism of breast cancer caused by estrogen exposure is caused by the stimulation of estrogen itself against the division of epithelial cells or by the hormone estrogen and its metabolites that directly act as mutagens. This hormone begins to be active when women first experience menstruation or menarche. Hormone levels of estrogen and early menarche can be affected by several aspects, such as lifestyle choices such as high-fat foods, low fiber, excess weight, and less physical activity.[5,12]

The longer the breast tissue is affected by harmful elements that cause cancer, such as chemicals, estrogen, or radiation, that can affect the process of cell proliferation, including cells in breast tissues. Early menarche will also cause multiple menstrual cycles and repeated estrogen increases and have a stimulating effect on mammae epithelial cells that can increase the likelihood of breast tissue abnormalities 4.24. Research by Rukmi and Handayani (2018) also found a link between menarche age and breast cancer in women. Women who experience their first menstruation at the age of <12 have a slightly higher risk of breast cancer than women who have menstruation >12 years old. The increased risk of breast cancer is due to the longer duration of estrogen exposure and higher levels of the estrogen hormone. When a woman experiences her first menstruation, the ovarian cycle that produces estrogen begins to function. The longer a woman is exposed to the hormone oestrogen is, the higher the risk of developing breast cancer will be. In addition, when exposed, the regularity of the menstrual cycle also plays a role. Cycle regularity describes a higher frequency of exposure compared to women whose menstrual periods are slower or have long menstrual cycles. Another study by Ningrum and Rahayu (2021) found similar results that there was a link between menarche age and breast cancer in women.[5,12]

History of use of contraception pills with breast cancer

In theory, the triggers of breast cancer from hormonal contraceptives are the hormones estrogen and progesterone. The use of hormonal contraceptives can increase the risk of cancer-related to hormonal factors, namely breast cancer and cervical cancer. In particular, it will significantly increase the use of CB-type or oral pills because oral contraceptives contains the hormone progesterone that, can affect the work of the estrogen hormone. The mechanism of the hormone estrogen stimulates the growth of ducts in the breast glands. Longer charging of the hormone estrogen can cause changes in the ductus cells in the breast glands. These changes can be abnormal hypertrophy and proliferation that can eventually turn into cancer.[24]

The results of this study showed that there was no association between the history of CB pill use and the incidence of breast cancer (p ≥ 0.05). The likelihood of this is due to respondents in the case group and the control group who used CB pills < 5 years, so the duration of exposure between the hormone estrogen and progesterone is not so long. Similarly, the menarche age in this study was dominated by respondents with the age of menarche ≥ 12 years, which was 34 people (63.0%). It shows that the duration of exposure to both estrogen and progesterone reproductive hormones has been associated with the incidence of breast cancer. In addition, the level of knowledge is dominated by good categories; there were 29 people (53.7%) in the case group or control group. The better a person's level of knowledge is, the more information they will receive that it affects the individual's behavior or health. The results of this study are consistent with Madjid *et al* (2022), who found no link between hormonal contraception and breast cancer in women. Hormonal contraceptives increase the risk of breast cancer but are not a significant increasing factor. Women who use oral contraceptives today have a quarter-fold greater risk than women who stopped using them 10 years ago, but the increased risk is statistically insignificant.[18]

Previous research suggested that using hormonal contraceptives for > 5 years could increase the risk of breast cancer by 1.52 times. It can occur due to the accumulation of the hormone estrogen in the body. This accumulation of estrogen can also lead to obesity due to increased levels of fat in the body. There was a 24% increase in breast cancer risk among oral contraceptive users. Users of oral contraceptives with high doses of estrogen may increase their risk of breast cancer by 10-30%.[6]

Relationship between knowledge level and breast cancer

The level of education of respondents also affects their mindset and scope of observation. The higher the educational level of the respondent is, the more the knowledge will increase. However, if they are less educated respondents, the less their knowledge will be because the level of education has an impact on behavioral changes and can produce many knowledge changes, especially in the field of health. A higher level of formal education will facilitate the absorption of information such as health so that the awareness of a person in healthy life behavior will be higher. Both in the case and control groups, the educational level of respondents was dominated by the level of primary education of 22 people (40.7%) and high school education of 20 (37.0%), while the educative level of the respondents of S1, was 12 people (22.2%). In this study, there was a link between the level of knowledge of the incidence of breast cancer and the OR value of 8.31.

The results of this study are consistent with Tambunan (2017) who stated that there is a positive relationship between the level of knowledge about SADARI (breast self-examination) and SADARI behavior. The higher the level of knowledge is, the better the behavior of the knowledge, and the lower the knowledge level of the information and the less the behavior of the understanding will be. The high rate of death from breast cancer is due to the fact that most cases come after advanced stages. It is due to several factors, including people who do not know or understand breast cancer, lack of attention to their breasts, fear of surgery, belief in traditional knowledge, and laziness and shame of showing breasts.[19]

Tiqiyah *et al.*, (2022) stated that there is a relationship between the level of knowledge of teenage girls and attitudes toward breast cancer prevention. Good knowledge has several factors that influence it, one of which is the age factor.[25]

Factors most associated with breast cancer

The most relevant variable in this study was the knowledge level variable, with a beta (β) exponent value of 7.859 times. In the case group, 19 respondents (70.4%) were found to have poor knowledge levels compared to the control group of 6 people (22.2%). Respondents with a low level of knowledge had a 7.859 times higher risk of developing breast cancer compared to those with a good level. The level of knowledge is the most dominant factor influencing behavior for early detection of breast cancer. Knowledge is the domain of psychology and becomes a predisposing factor that becomes an individual's consideration in facilitating and underlining the occurrence of certain behaviors. Actions based on knowledge that a person possesses will last longer than actions that are not based upon knowledge. When a woman has a good knowledge of the importance of early detection of breast cancer, i.e., the presence of abnormal bumps in the breast, there will be a positive response to behavior. However, if the knowledge is insufficient, it will not produce a good response to conscious behaviour.[26,27]

Factors that influence knowledge, among others, include education. The higher a person's education is, the more a person is able to receive and understand information. Information or mass media also play a role. If information about a lesson is obtained often, it will increase knowledge and awareness, while a person who rarely receives information will not increase his knowledge and wisdom. A person with good social and cultural knowledge will have more awareness. However, if his social culture is not good, neither is his knowledge. Economic status affects the level of knowledge because someone who has an economic status below average will find it difficult to add knowledge. Environment affects the process of entering knowledge into the individual due to the presence of mutual interaction that will be responded to as knowledge by the individual. If the environment is good, then the knowledge obtained will be good. However, if the environment is not good, then the science acquired will also be bad. If an educated person surrounds a person, then the knowledge a person has will be different from that of an unemployed and uneducated person. The experience factor is how to solve problems from previous experience so that the experience gained can become knowledge to solve problems. Age factors: as one ages, one's understanding and thinking will also develop so that the knowledge acquired will also increase.[8,21,27]

The sufficient level of knowledge that respondents had in this study could be due to the fact that almost all respondents have been exposed to information about breast cancer prevention efforts. The good

knowledge that respondents have is influenced by educational factors and also due to the age factor. The older they are, the more they develop their capability and mindset. The age range of respondents is predominantly between the ages of 31 and 40. A woman's risk of breast cancer can be greater in her 30s to 40s. As a woman ages, the fat cells in the breasts tend to produce large amounts of the aromatase enzyme, which will eventually increase local estrogen levels. This locally produced estrogen is believed to play a role in triggering breast cancer in postmenopausal women. Once a tumor is formed, the aromatase enzyme will increase the level of estrogen to trigger the tumor to grow into cancer.[8,27]

CONCLUSION

There was a relationship between age at menarche and knowledge level about breast cancer incidence at the Department of Oncology Surgery at Dr. Doris Sylvanus Hospital Palangka Raya. There was no association between a history of contraceptive pill usage and breast cancer occurrence among women. The most dominant factor associated with breast cancer occurrence was the level of knowledge. Increasing knowledge about cancer is important in preventing breast cancer in women, especially in Palangkaraya.

CONFLICT OF INTEREST

The researcher declares that he has no affiliation or involvement in any organization or entity with any financial or non-financial interests.

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