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Systematic Review

RISK FACTORS AFFECTING THE EVENT OF BREAST CANCER IN SOUTHEAST ASIA

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A B S T R A C T

Background: Breast cancer is one of the reproductive cancers that cause increased morbidity and mortality. Based on the Global Burden Cancer (Globocan) data, breast cancer has increased by more than 20%, while the mortality rate has increased by 14% since 2008.

Purpose: The aim of the study is to conclude a systematic literature review that is related to risk factors that influence breast cancer in Southeast Asia.

Methods: This study emphasizes risk factors that influence breast cancer incidence such as; contraceptive use, age, body mass index, menarche, menopause, parity, breastfeeding, and smoking using the systematic literature review method identified a total of 7 relevant journals and summarized in a narrative manner.

Result: The results of this journal review show that contrast use, age, body mass index (BMI) in this case a higher BMI or obesity, early age menarche that is influenced by unhealthy lifestyles, menopause, and the Human Papillomavirus (HPV) significant risk factors that influence breast cancer incidence in Southeast Asia.

Conculison: Age, body mass index (BMI), and the contraseptive use very influential on the incidence of cancer.

INTRODUCTION

Reproductive cancer is a cause of worldwide morbidity and mortality that threatens women's health and life [1]. Research conducted by Ferlay et al (2014) in the journal Wang et al., [1] suggests that the most common reproductive cancer in women is breast cancer, with an incidence of 1.67 cases diagnosed worldwide in 2012. Based on the Global Burden Cancer (Globocan) report, breast cancer has increased by more than 20%, while the mortality rate has increased by 14% since 2008.

Research results in Malaysia by [2] reported that breast cancer is the most frequent cancer in Peninsular Malaysia, with an incidence rate of 31.3% and continues to increase, whereas in Thailand the results of the study [3] showed the highest incidence of breast cancer in Bangkok at 34.1% and the lowest in Nakhonphanom, like other countries, breast cancer is still a public health problem for Thai women.

The prevalence of cancer in Indonesia is 40.3 / 100,000 cases, with a mortality rate of 16.6 / 100,000 cases and is the highest inpatient cases with 12,014 cases. The incidence of breast cancer in Indonesia is influenced by age, menarche, menopause, birth status, breastfeeding, obesity, unhealthy diet, having had breast tumors, family history of breast cancer [4].

Epidemiological studies and risk factors for breast cancer are very important for prevention. The use of hormonal contraception is a risk factor for breast cancer, but the magnitude of the risk is unclear. Other risk factors that influence the incidence of breast cancer are; "age, body mass index, family history of breast cancer, early menarche, and menopause, age at first birth, and time of breastfeeding [3].

Human papilloma virus (HPV) is also a risk factor for breast cancer, a molecular epidemiological study conducted, has

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collected data relating to Human papilloma virus (HPV) with breast cancer and shows that HPV is present at high frequencies in breast cancer samples, and rarely found in normal breasts [5].

The purpose of the Systematic literature review is to find out "risk factors that influence the incidence of breast cancer in Southeast Asia.

METHOD

This research is a kind of systematic literature review research, which uses the methodology proposed by Peters et al [6] to determine and align research goals and questions, create inclusion criteria, explain the approach used in article disbursement.

The review question in this systematic literature review is "risk factors that influence the incidence of breast cancer in Southeast Asia. Researchers followed JBI guidelines using the Population, Intervention, Comparison, Outcomes (PICO) framework, as a reference in identifying keywords that fit the purpose of the review question [7]

Table 1. Framework PICO

Kriteria	Inklusi	Eksklusi
Population/ Problem	Women with breast cancer in Southeast Asia	Women with breast cancer outside Southeast Asia
Intervention	Risk factors that influence the incidence of breast cancer	
Comparison	Women with breast ıncer a and cervical ıncer	
Outcomes	Breast cancer	

Disbursement strategy is to find articles that are published are limited to English and published in 2014-2019. The article search uses several relevant databases that is PubMed, ScienceDirect, EBSCO, Proquest.

RESULT and DISCUSSION

Search result

The findings obtained through a systematic search obtained by journals published 2014-2018, authors and data sources taken from several countries in Southeast Asia that is; Singapore (n = 2), Malaysia (n = 2), Indonesia (n = 1), Thailand (n = 2). There were 7 journals found with Q1 = 5 journals, and Q2 = 2 journals. All journals use Quantitative methods with several types of approaches or mix methods.

DISCUSSION

Globally, breast cancer is a cancer that often occurs and the most common cause of death among women. The incidence and death from breast cancer in high resource countries is decreasing while in low resource countries it is increasing. Risk factors for breast cancer include age, race, history of menarche, breast characteristics, hormonal use, alcohol, tobacco, diet, physical activity, and lifestyle [11]. Breast cancer is prostatic cancer that can affect other organs such as bones, liver, lungs and brain and cannot be cured. Risk factors such as sex, aging, estrogen, family history, gene mutations and unhealthy lifestyles can increase the likelihood of breast cancer [12]. Breast cancer is more often associated with environmental, reproductive, and lifestyle factors, and 10% of breast cancer can be associated with inherited genetic mutations [13].

Based on a review of articles showing that risk factors for breast cancer events in Southeast Asian countries are caused by contraceptive use, age, body mass index, menarche, menopause, HPV. This in line wiht research by Nindrea et al., (2017) a risk factor for breast cancer in women in Southeast Asia is parity, body mass index, and use of oral contraceptives and this factor can still be modified, while some factors that cannot be modified are family history of breast cancer, age and menopausal status. Research [15] also mentioned the same thing that age of menarche, menopause, parity, hormone use and physical activity were significantly associated with also mentioning the same thing that age of menarche, menopause, parity, hormone use and physical activity were significantly associated with breast cancer. Being overweight and using oral contraceptives contribute to an increased risk of breast cancer [16]. Being overweight and using oral contraceptives contribute to an increased risk of breast cancer [12] that there is an increased risk associated with early menarche and menopause. Beberapa hasil artikel yang peneliti Some of the results of the article that researchers found outside of the review mentioned the same results as what was reviewed related to risk factors for breast cancer in Southeast Asian countries, but not found that HPV is a risk factor for breast cancer. HPV is still a matter of debate whether HPV is a risk factor for breast cancer. Research [17] did not show a correlation between HPV and breast cancer. Not Found HPV DNA identified in breast cancer samples, however the results in the study stated that patients with cervical samples positive for HPV were more likely to have tumors with positive progesterone receptors. According to [18] Although the risk factors for breast cancer are well known, early menarche, menopause, the underlying cause of breast cancer is unknown. The development of substantial recent evidence suggests that some viruses may have a role in breast cancer. These viruses

include HPV, but it is said that HPV and breast cancer are substantial but not conclusive evidence. This is still in line with research [19] that the causal relationship between HPV and breast cancer is controversial. But more and more evidence shows that HPV can play a key role in the invasion of breast cancer, the presence of HPV is associated with increased tumor development [20]. The researchers' assumption in this regard is that HPV is not a risk factor for breast cancer, however, it can occur in women with a history of cervical cancer which can have implications for the development of several types of breast cancer. The presence of HPV is associated with tumor development.

CONCLUSION

Based on the results of a review of several articles mentioning that contraceptive use, age, body mass index, menarche, menopause, HPV are risk factors for breast cancer in Southeast Asia, but based on a broader review of the article there are similarities related to breast cancer risk factors, only not found HPV is a significant risk factor for breast cancer. There are still a number of controversial articles. Also related to body mass index has not been found in greater clarity whether the body mass index referred to in this article is obesity or others. Some articles mention that early menarche is a risk factor for breast cancer, just not explained in detail what is the cause so women with a history of early menarche are at risk of developing breast cancer.

Health workers in supporting the incidence of breast cancer, by further increasing the provision of health education about the importance of early detection of breast cancer. It is important for medical personnel to know the risk factors for breast cancer in order to be able to provide education, especially for women at risk who want to use hormonal contraception.

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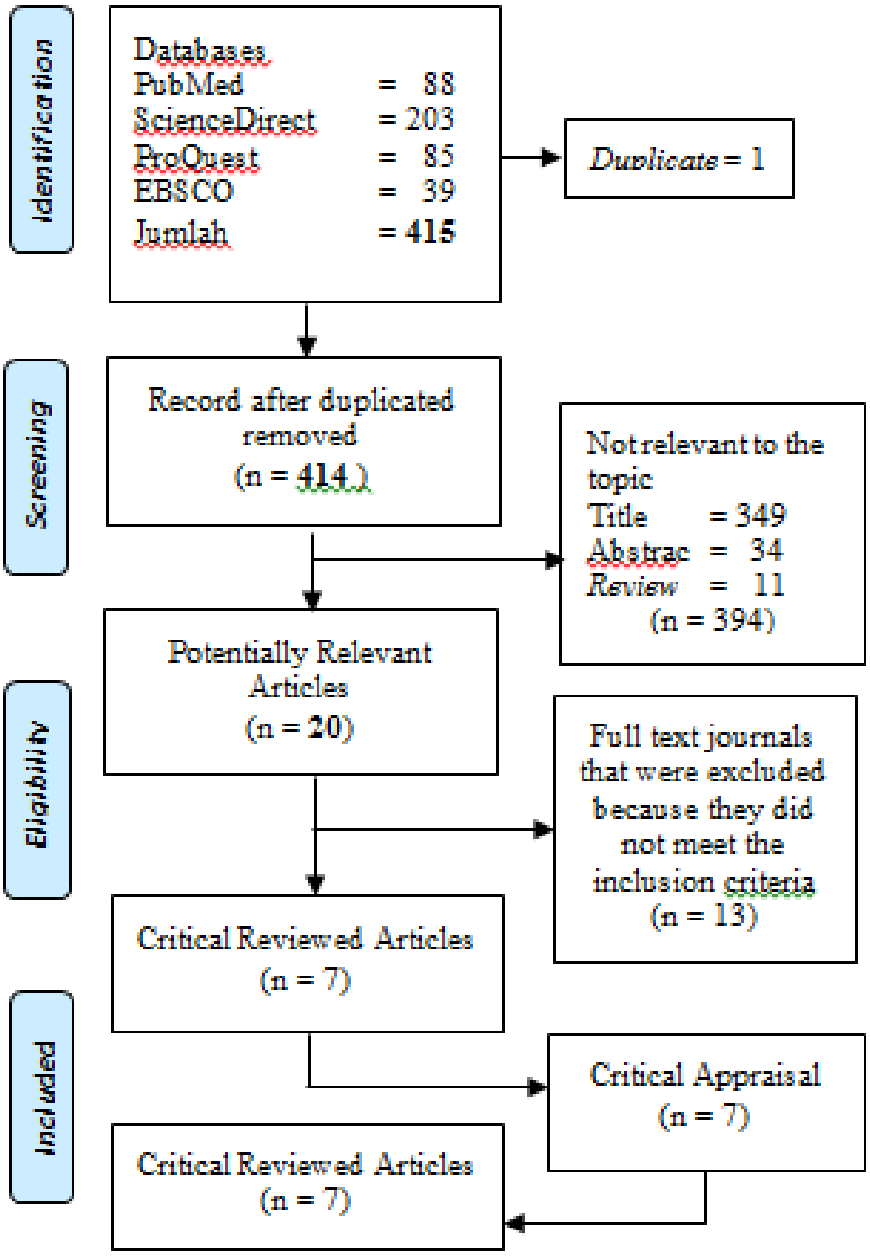
Chart PRISMA Flowchart

Gambar 2.1 PRISMA *Flowchart*



Data Extraction Analysis

No.	Title	Author/Year	Types of Reserch/ Participant	Result
1	Temporal trends of common female on breast, cervical and ovarium cancer mortality in Japan, Republik Korea and Singapore;	Wang et al /2018	Quantitative / WHO Mortality Rate in Japan Republic of Korea and Singapore, not included in the total population	Risk factors in Singapore for the effects of age continue to increase in the age group of 20-54 years, and it is increasing constantly in all age groups from 20 to 79 years and the lowest is 75- 79 years.
2	In vivo and in vitro studies a posible involvement of HOV infection in the early stage of breast carcinogenesis via APOBEC3B induction, Singapura	Ohba et al/ 2014	Quantitative / 209 breast cancer specimens.	High risk of detectable HPV DNA 31% of all breast cancer samples. The relationship of breast cancer and HPV depends on age. Positive HPV was lower when patients were young and increased due to age (p = 0.1155).
3	A case-control study of breast cancer risk factors in Malaysia	Tan et al/ 2018	Quantitative / 3683 case group and 3,980 control group	Family history of breast cancer is associated with an increased incidence of breast cancer, menopausal women have a 52% increased risk of breast cancer . The use of oral contraceptives is not significantly associated with the risk of breast cancer. Body mass index is more associated with a lower risk of breast cancer . There is no significant relationship between smoking status and breast cancer in women.
4	Oral contraceptive and breast cancer; a case control study in six referral hospitals in Indonesia	Wahidin et/ 2018	Quantitative / 381 case group with breast cancer and 381 control group	Use of oral contraceptives> 6 years is 1.5 higher in the case group . The use of oral contraceptives <6 years is 2.4 times higher in the case group . The age factor is more in the case group aged 40-49 years . Obesity is more in the case and control groups . Family history is 1.2 times higher in the case group. Use of oral contraceptives> 6 years shows an increased risk of breast cancer (p = 0,000) with an OR value of 90. Use of <6 years 1.79 times more risk. Early menarche significantly influences breast cancer.
5	Hormonal contraceptive use and breast cancer in Thai Women/ Thailand	Poosari et al/ 2014	Quantitative / 11,414 respondents	Hazard Ratio (HR) subgroup analysis for breast cancer with the use of hormonal contraception in women younger than 50 years of age is 0.86 (95% CI, 0.30-2.45), whereas in women> 50 years (95% CI 0.75-4.88). Hormonal contraception (oral; HR = 1.35, 95% CI, 0.65-2.78; HR injection = 1.25, 95% CI, 0.58-2.80) and there is no relationship between the duration of contraceptive use hormonal with breast cancer.
6	Ethnic differences in mammographic densities; An Asian Cross-sectional study /Malaysia	Mariapun et al/2015	Quantitative / 1,240 respondents	Body mass index, parity, age at the beginning of pregnancy, 12 months of breastfeeding and menopausal status were significantly associated with breast cancer . Age, body mass index, menopause status, parity accounted for 16.1% of breast cancer .
7	Development and of a breast cancer risk prediction model for Thai Women; A cross sectional study/ Thailand	Anosthaisintawe et al/	Quantitative / 17,506 respondents	Age, menopause status, body mass index and use of oral contraceptives are significantly associated with breast cancer

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Risk Factors that influance the incidence of breast cancer in Southeas Asia

No.	Risk Factors Breast Cancer	Result
1.	Contraceptives use	From the review results it was found that the use of contraception is a risk factor for breast cancer. Some articles mention there is a relationship between the use of oral contraceptives with the incidence of breast cancer in Indonesia. The use of oral contraceptives ≥6 years can increase the risk of breast cancer (p = 0,000) with an OR value of 99, meaning that the use of oral contraceptives is significantly a risk factor for breast cancer and 99 times the risk compared to those who have never [4]. The duration of oral contraceptive use and hormone replacement therapy has an impact on the incidence of breast cancer [8]. The use of oral contraceptives is significantly associated with breast cancer [9] However, there are articles that mention that the use of hormonal contraception is not related to the risk of breast cancer and no type of contraception was associated with a significant risk of developing breast cancer and there was no relationship between the duration of contraceptive use and breast cancer [3]. This matches what was found in the article [10], that the use of oral contraceptives was not significantly associated with the risk of breast cancer
2.	Age	The age factor accounts for 15.1% of breast cancers. Older age is significantly related to breast cancer. An average age of 50-51 years was found in breast cancer sufferers in Malaysia in ethnic Chinese and Indians [8]. Age less than 54 years is more commonly found in breast cancer sufferers (Tan et al. 2018). The age factor for breast cancer sufferers in Singapore continues to increase in the 20-79 years group, and begins to decline in the age group 75-79 years [1]. As for Thailand, the age of breast cancer sufferers is 54 years and for reproductive age found at the age of 14 years. About 70% of menopause women age 48 years suffer from breast cancer [9]. As for Indonesia also found similar things where the age of 40-49 years was more commonly found in the group of breast cancer cases [4]
3.	Body mass index (BMI)	Some articles found show that body mass index is a risk factor that influences the incidence of breast cancer. BMI accounts for 16% of causes of breast cancer [8]. BMI that affects breast cancer is obesity. Obesity is a significant predictor of breast cancer with an OR value of 2.02, artinya orang dengan obsesitas 2 kali lebih berisikp mengalami kanker meaning that people with obsessions are twice as noisy as breast cancer [9]. BMI that exceeds the normal limit or called obesity is influenced by unhealthy eating patterns 1.2 times higher risk of developing breast cancer [4].
4.	Menarche	Early menarche (<13 years) has a significant relationship with breast cancer [4]. Anothaisintawee et al., (2014) found no significant results between early menarche and breast cancer. Tan et al., (2018) found no significant association with menarche and breast cancer.
5.	Menopause	Postmenopausal status is defined as no menstruation during the past year. Postmenopausal women have a 52% increased risk of breast cancer [1]. Women older than 60 years have a higher risk of developing breast cancer, and premenopausal women about 90% higher breast cancer than postmenopausal women [9].
6.	Human Papilloma Virus (HPV)	One of the articles found revealed the association of Human papilloma virus (HPV) with breast cancer. Where a molecular epidemiological study was carried out has collected data relating to HPV and breast cancer. In this article it is mentioned that HPV is found mostly in breast cancer samples, and rarely found in normal breasts. However, the results of this study are still varied and even conflicting. Although some authors from previous studies suggest the etiological role of HPV in breast cancer, but there is no clear explanation offered for the mechanism of other causes of high positive HPV as the only reason that HPV is a cause of breast cancer [5].