Risk factors in the development of breast cancer among Indonesian women

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Abstrak

Telah dilaksanakan suatu penelitian kasus-kontrol dengan 300 triplet untuk mengidentifikasi faktor risiko terjadinya kanker payudara di kalangan wanita Indonesia. Dari dua belas faktor risiko yang di analisa secara univariate terdapat enam faktor yang secara bermakna berkaitan dengan kejadian kanker payudara. Analisa lebih lanjut dengan pendekatan regresi logistik menunjukkan bahwa adanya lima faktor risiko yang mempunyai pengaruh nyata dalam pertumbuh kanker payudara, yakni keterlambatan menars (OR 2,35 CI 1,60-3,44), laktasi jangka pendek (OR 2,21 CI 1,02-4,78), trauma payudara (OR 1,98 CI 1,12-3,49), konsumsi lemak berlebihan (OR 1,81 CI 1,30-2,52), dan menopause (OR 1,54 CI 1,15-2,05).

Abstract

A case-control study to identify risk factors on the development of breast cancer among Indonesian women has been conducted using 300 triplets. Twelve potential determinant factors have been assessed using uni-variant analysis, and six of them showed significant association with breast cancer. Further analysis using logistic regression method revealed that five factors, namely late menarche OR = 2.35 (1.60-3.44), short lactation OR = 2.21 (1.02-4.78), breast trauma OR = 1.98 (1.12-3.49), excessive fat consumption OR = 1.81 (1.30-2.52), and menopause OR = 1.54 (1.15-2.05) have real effect on the development of breast cancer.

Keywords: Case-control study, risk factor, breast cancer, epidemiology.

INTRODUCTION

In Indonesia, intensive public health program in controlling acute communicable diseases and nutritional problems has lead to significant improvement of health condition. Incidence rates of many major communicable diseases have decreased, and life expectancy has increased. On the other hand, chronic diseases such as cardio-vascular and malignancies started to show significant impact on the ten leading causes of death.[1-4] Breast cancer ranked the second among Indonesian females; with slightly increasing trend of its specific incidence rate observed within 5 years pathology based cancer registry from 1988 up to 1992.[5]

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Malignancy creates the most severe psychological impact to the family members compared to other chronic diseases. Breast cancer is the second highest of malignancy among the Indonesian women just after the cervical cancer. The majority of diagnosed and treated cases in the General Hospital came in late stages, thus lowering the five-year survival rate.[6] Intensive public education program must be developed using a multi disciplinary approach.

There are many factors, which have been studied in the developed countries as having significant role on the development of breast cancer. High consumption of fatty food, hormonal use, breast trauma, menopause, and genetic traits showed causal relationship with breast cancer among women in the affluent countries.[7-24] On the other hand the practice of long-term lactation can reduce the risk of breast cancer.[25-33] The Indonesian local diet tends to content excessive saturated fatty acids, both animal and vegetable sources.[38] With the difference on environmental conditions and the way of life, there is a need to confirm whether these risk factors also played important role among Indonesian women. This study was intended to identify significant risk factors on the development of breast cancer in Indonesia and assessed their rank of influence.

MATERIALS AND METHODS

A case-control study design with 1:2 ratio was applied in this assessment. Two types of study subjects were used in this study. The patients were defined as all newly diagnosed breast cancer patients who came to Jakarta General Hospital during the study period of 1989 to 1992. Almost all of breast cancer patients in the area, especially those from middle to lower socio economic level, will be referred to this hospital. The diagnosis of breast cancer was performed either histopathologically or using Ultra Sound/Mammography.[6,35]

The controls were defined as non-breast tumor and non-malignancy patients who came for medical assistance to the surgery or other departments of the General Hospital during the study period. For every breast cancer patient there were two hospital controls at the same age range to increase its statistical power. Using a 95% confidence limit, statistical power of 80% and assumed relative risk of two times, with an average 40% of risk factor's exposure rate, this study has recruited 300 cases and 600 controls in a single hospital.

Demographic characteristics of the respondents were gathered through a structured interview, while medical data were collected through physical examination. Nutritional data were collected and probed indepthly using a simple food model. Since the control must be free from any breast tumor, the trained paramedics also examined the respondents through breast palpation to exclude controls with breast lump.

The twelve risk factors which were included in this study are present weight, age at first sexual contact, parity, education, late menarche, menopause, hormonal use, breast trauma, lactation, genetic trait, fat and protein consumption. Each potential risk factor was assessed through uni-variant analysis and was measured its estimated Relative Risk and the 95% confidence intervals. For all significant risk factors, a further analysis has been applied to assess the strength of association for each determinant factor given that all other factors retained as constant. Logistic regression method was selected for this multi-variate analysis.[36]

Excessive fat and high protein consumption was defined if the subject consumed more than 4 days per week at usual food-size. Low educational level was defined for those who only had elementary education. Late menarche was defined for subject who experi-

enced menarche at the age of 16 years or later. Short-term breast-feeding was defined for subject who has a total breast-fed period of less than 6 months.

RESULTS

Age distribution of cases and controls showed that the majority of study respondents came from 30 to 49 years age group, 54% for cases and 53% for controls. There are small percentages of cases and controls that aged less than 30 years. Old respondents who aged more than 69 years comprised of 3% for cases and 2.5% for controls. The average age of cases is 47 ± 11.9 years, while for controls is 46.9 ± 12 years (see Table 1).

Table 1. Age distribution of cases and controls

Age distribution	Cases (n=300)	Controls (n=600)
Under 30 years	4.7 %	5.0 %
30 - 39 years	23.3 %	27.8 %
40 - 49 years	31.0 %	25.8 %
50 - 59 years	18.3 %	20.8 %
60 - 69 years	19.7 %	18.0 %
Above 69 years	3.0 %	2.5 %
Mean age and S.D	47.0 ± 11.9	46.9 ± 12.0

Among the 300 breast cancer cases, 80% of them came at the late stages. More than 57% of breast cancer cases are already at the III-B or more severe stage which have low response to the available treatment.

Table 2. Clinical stage of breast cancer cases

Clinical stage	Number	Percentage
Stage I	14	4.7
Stage II	46	15.3
Stage III-A	68	22.7
Stage III-B	116	38.7
Stage IV	56	18.6
TOTAL	300	100.0

The selection of controls did not interfere with the possible determinant factors. No control subject was diagnosed of having any disease, which has confirmed causal association with any potential factor, whether increasing or decreasing association (see Figure 1). The majority of control group were healthy women who visit the hospital for consultation. Thirty-four percents of control visited surgery department seeking medical assistance for ordinary medical problems.
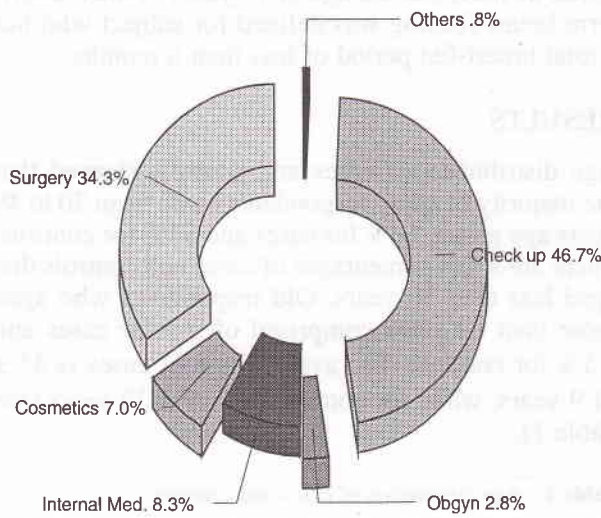
Figure 1. Clinical diagnosis of controls

Uni-variant analysis of determinant factors showed that only six of them have significant role on the development of breast cancer and need further analysis. Table 3 shows that present weight and the age at first sexual contact did not have significant correlation with the development of breast.

Table 3. Body weight and age of sexual activity compared between breast cancer cases and controls

Factors	Cases		Controls		p
	Mean	SD	Mean	SD	
Weight	50.5	14.2	51.0	14.2	0.569
1st sexual age	19.7	4.6	19.9	3.9	0.578

Tables 4 and 5 show that educational level and parity status were not significantly linked with breast cancer risk, eventhough low or no education appeared to increase the risk by 1.18 and 1.24 times.

Table 4. Impact of educational level to breast cancer

Education level	Cases	Control	OR
Middle education	114	256	
Low education	108	195	1.24 (0.90-1.72)
No education	78	149	1.18 (0.83-1.67)
Total	300	600	

Table 5. Impact of parity status to breast cancer

Parity status	Cases	Control	OR
No parity	43	84	
1 - 3 parity	134	256	1.02 (0.67-1.56)
4 + parity	123	260	0.92 (0.60-1.41)
Total	300	600	

Table 6 shows an association between lactation and breast cancer. Those women who never breast-fed only showed a slight increase of risk, but it is not a significant association. On the other hand, those women who breast fed for less than 6 months significantly experienced a 2.6 times risk.

Table 6. Impact of breast-feeding to breast cancer

Breast-feeding	Cases	Control	OR
Long period	231	490	
Short period	16	13	2.61 (1.27-5.38)
Never brestfed	53	96	1.17 (0.80-1.68)
Total	300	600	

Table 7 shows that hormonal drug use such as contraceptive methods appeared to affect the development of breast cancer. There was no significant relationship of genetic trait with this kind of malignancy. Late menarche has the second strongest causal relationship with a relative risk of 2.3 times just behind short-term breast-feeding. The experience of physical breast trauma also shows significant impact on the development of breast cancer. Women who already are menopause or those who consumed excessive fatty food and high protein diet show higher risk of developing breast cancer compared to average women.

Table 7. Impact of other factors to breast cancer

Factors	Cases		Control		OR
	+	−	+	−	
Late menarche	67	233	66	534	2.33 (1.60-3.38)
Breast trauma	26	274	28	572	1.94 (1.12-3.37)
Menopause	163	137	271	329	1.44 (1.09-1.91)
Hormonal drug	38	262	52	548	1.53 (0.98-2.38)
Genetic trait	53	247	92	508	1.19 (0.82-1.72)
Excessive fat	97	203	118	482	1.95 (1.42-2.67)
High Protein	193	107	342	258	1.36 (1.02-1.81)

When logistic regression analysis method was applied for the six significant risk factors, high protein consumption did not show real impact on breast cancer. By keeping other risk factors constant, the causal relationship of high protein diet diminished. Late menarche, breast trauma, menopause remained as significant as short-term lactation and consumption of excessive fat.

Table 8. Estimated Relative Risk of determinant fa .ors

Factors	Uni-variant	Multi-variant
Late menarche	2.33 (1.60-3.38)	2.35 (1.60-3.44)
Breast trauma	1.94 (1.12-3.37)	1.98 (1.12-3.49)
Menopause	1.44 (1.09-1.91)	1.54 (1.15-2.05)
Short lactation	2.61 (1.27-5.38)	2.21 (1.02-4.78)
Excessive fat	1.95 (1.42-2.67)	1.81 (1.30-2.52)
High protein	1.36 (1.02-1.81)	1.24 (0.91-1.67)

DISCUSSION

As one of the most prevalent female malignancies in the world, there were many researches have been conducted on breast cancer. Long list of confirmed determinant factors have been revealed through series of worldwide efforts of researchers. These determinant factors can be classified into two categories, namely precipitating factors and protecting factors.[41-43]

This case control study has been conducted to confirm causal relationship of twelve important determinant factor\s with the development of breast cancer among Indonesian women. Unlike women in the developed countries, the Indonesian women tend to differ in many aspects such as genetically, physically, culturally, and socio economically.[42-48] These differences have affected also the way of known determinant factors in influencing the development of breast cancer.

Uni-variant statistical analysis showed that body weight and age at the first sexual contact do not have any impact on the development of breast cancer among Indonesian women. The average body weight among the Indonesian women tends to be much less compared to women in the developed countries.[45, 46] Obesity, which is related to excessive fat accumulation, has not been found to be significant factor in this study.

The education level, parity status, hormonal drug use and genetic trait did not show any effect on the de-

velopment of breast cancer among Indonesian women. Calculation of Odds Ratio and its 95% confidence interval showed that these variables need not to be pursued further in a multi-variant analysis. Unlike previous allegation, the use of hormonal drugs such as contraceptive methods did not affect this malignancy. Other variables such as excessive fat or protein consumption, menopause status, late menarche, short-term lactation, and breast trauma gave Odds Ratio which significantly higher than one and need to be included in the logistic regression analysis.

Excessive fat consumption, menopause, late menarche, short-term lactation, and breast physical trauma show constant high risk of developing breast cancer. The level of Odds Ratio of these constant factors did not differ significantly after multi-variant analysis. On the other hand, excessive protein consumption diminishes its influence after being controlled by other determinant factors. This finding showed that actually protein consumption does not affect the development of breast cancer, but it tend to blend with high fat consumption.

Many previous studies gave strong evidences of long-term breast-feeding as protecting factor of breast cancer.[25-33] In this study, long-term lactation of more than 6 months did not show enough significant reduction of risk. On the other hand, short-term lactation has raised the risk significantly compared to those who breast-fed longer. The theory of premature braking of endogenous hormonal factors was assumed to have effect in this situation. Once the baby has sucked the papillae and induced active production of hormonal, the process can not be reversed drastically. The mammary gland cells that have been forced to produce milk by this hormone, needs time in adjusting themselves when the mother start to wean the baby. If this induction was stopped abruptly, the endogenous impact is very great and creates the uncontrolled proliferation of mammary gland cells.

In short, this study revealed the following major findings. a) The majority of hospitalized breast cancer cases in Indonesia were on the late stages, b) The study has identified precipitating risk factors such as late menarche, breast trauma, excessive fat consumption, and menopause, c) The early weaning process tend to precipitate breast cancer development.

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