Epidemiological Analysis of Risk Factors for Breast Cancer in Indonesian Females

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Abstrak

Untuk menetapkan faktor-faktor risiko pada perkembangan kanker payudara dilakukan penelitian epidemiologik selama 3-tahun yang termasuk pada penelitian kerjasama antara Indonesia dan Jepang. Metoda kasus-kontrol dipilih dan digunakan penderita yang mengunjungi Rumah Sakit Pusat Nasional Dr. Cipto Mangunkusumo, Jakarta. Tiga ratus kasus kanker payudara yang baru dan diperkuat dengan pemeriksaan histopatologik diadu berpasangan, menurut umur (+/- 3 tahun) dan status sosioekonomik, dengan 600 kontrol. Data yang dikumpulkan adalah data demografik, pajanan terhadap radiasi, hubungan genetik, pola makanan dan kebiasaan hidup lainnya. Analisa data dilakukan dengan cara univariat. Hasilnya menunjukkan bahwa beberapa faktor meningkatkan risiko kanker payudara, yaitu trauma pada payudara, berat badan rendah, menopause yang alamiah, menopause yang diinduksi, jumlah kehamilan rendah (1-2 kali), masa menyusukan bayi yang singkat (kurang dari 4 bulan), hubungan keluarga dekat dengan penderita kanker payudara dan konsumsi makanan berlemak. Faktor-faktor yang menurunkan risiko kanker payudara adalah status perkawinan yang berpisah, keadaan menduda, berat badan berlebihan, siklus haid tidak teratur. Disimpulkan bahwa faktor risiko yang paling mencolok adalah 1). menopause yang diinduksi dan 2). masa menyusui bayi singkat (kurang dari 4 bulan) (Risiko Relatif masing-masing 5.96 dan 5,44). Peningkatan risiko kanker payudara dua sampai tiga kali pada keadaan berat badan rendah dan konsumsi makanan berlemak (Risiko Relatif masing-masing 2.85 dan 2.63). Oleh karena konsumsi makanan berlemak merupakan salah satu faktor risiko yang bermakna, penelitian diperpanjang dengan analisa gizi yang lebih lanjut.

Abstract

To identify risk factors in breast cancer development a 3-year epidemiological study was carried out in the joint research project between Indonesia and Japan. Case-control method has been chosen and patients visiting Dr. Cipto Mangunnkusumo National General Hospital, Jakarta were used. Three hundred cases, newly diagnosed primary breast cancer patients, confirmed with histopathological examination were matched by age (+/- 3 years) and socio-economic status with 600 controls. Data collected were demographics, reproductives, breast trauma, radiation exposure, genetical traits ,dietary pattern and other lifestyles. The epidemiological data were analyzed by univariate method. The results showed that several factors increased breast cancer risk, namely breast trauma, underweight, naturally occuring menopause, induced menopause, infrequent (1-2 times) pregnancy, short period (less than 4 months) breast feeding, close genetic trait with breast cancer patient and fatty food consumption. Factors reducing the risk of breast cancer were separated marital status, widowed, overweight and irregular menstrual cycle It was concluded that the most prominent risk factors were 1) induced menopause and 2) short period (less than 4 months) breast feeding (Relative Risk of 5.96 and 5.44 respectively). The risk of breast cancer was twice to thrice in patients with underweight, among close genetic traits and those consuming fatty food (Relative Risk of 2.2, 2.85 and 2.63 respectively). Since fatty food consumption was found as one of the significant risk factors, the study has been extended with further nutritional analysis.

Keywords: *case-control study, risk factors, breast cancer*

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According to the last demographic census, Indonesian women experience longer life expectancy than ten years ago. Live longer means a higher possibility of manifesting chronic diseases. The last health statistics from Ministry of Health[1] showed an increasing rank of chronic diseases morbidity and mortality. Cancer ranked the fifth in morbidity and the third in mortality. In women, breast cancer ranked the second after cervical cancer,[2,3] with relative frequency around 18% in pathology based and limited population based cancer registry.

Many factors incriminated as having influences on the development of breast cancer.[4,5] Changing life styles, long- term use of hormonal contraceptives and certain type of diet are known as potential risk factors. These behavioral changes are believed to have significant impact on the probability of contracting breast cancer in Indonesia as well. Some potential risk factors have been looked upon in descriptive study incorporated in clinical investigation.[6]

Most of the patients diagnosed as having breast cancer, were already in the late stages, and thus markedly reduced the efficiency of surgery, chemo- and radiotherapy. In order to improve the quality of health services including preventive measures for breast cancer, health managers need to have a clear and accurate information on which factors affect the development of this malignancy. Since various epidemiologic studies[4,5] have been conducted in other populations, it is of importance to study risk factors in breast cancer development among Indonesian women. It is expected to look upon both the similarity and the dissimilarity with the accompanying study in Japanese women and other data.

The general hypothesis for this study was that Indonesian women with more modern life style will show a higher probability of getting breast cancer. Specific objectives of our study include a possible association of breast cancer with reproductive history, breast traumas, exposure to hormonal contraceptive, frequent exposure to radiation, close genetic traits and imbalanced dietary pattern.

METHOD

The study design adopted in this study was a CASE-CONTROL study design[5,7] with a double matched control groups. The Dr. Cipto Mangunkusumo National Central General Hospital served as a source of cases and controls. Data collection from cases and controls had been carried out for 3 years, from November 1988 to December 1991.

Eligible cases in this study were women who had been newly diagnosed as having primary breast cancer, irrespective of its clinical stage. The diagnosis was made by histopathological examination of biopsied tissue. Matched controls were recruited from surgery department or other department of the same hospital.

Population for controls were women who were confirmed as having neither breast cancer nor lumps, and matched to the cases by age (+/- 3 years), and socio-economic status, by the room category of hospitalization. Controls were collected twice as many as cases with 3 months recruitment phase for each triplet.

Based on statistical consideration (α= 0.05 and β= 0.2) 300 triplets were colected.

Cases and controls were interviewed by two well trained nurses, using standardized questionaires. The questionaire were edited in advance by a supervisor before tabulation.

The case and control groups were tested for comparability on age and some socio-economic variables. Relative risk (RR) was estimated by computing the Odds ratio (age adjusted or adjusted for confounders by regression analysis). The significance of the RR was determined based on 95 % confidence interval (CI).

RESULTS

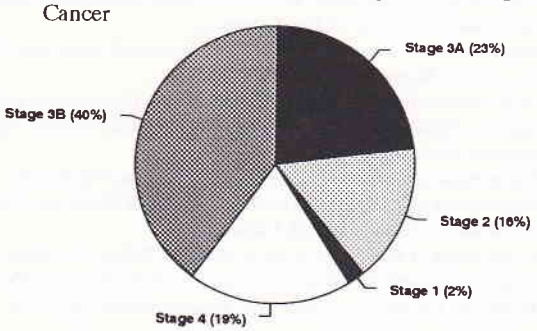
The age distribution of the study subjects are given in Table 1. Mean ages were 46.9 for both cases and controls indicating no statistical difference and were well matched for age.

Table 1. Distribution of age among cases & controls

Age (yrs)	Cases		Control	
	n	%	n	%
< 35	51	17	104	17.3
35 - 39	34	11.3	93	15.5
40 - 44	51	17	71	11.8
45 - 49	42	14	84	14
50 - 54	29	9.7	64	10.7
55 - 59	26	8.7	61	10.2
60 - 64	46	15.3	73	12.2
65 - 69	12	4	35	5.8
> 70	9	3	15	2.5
Total	300		600	
Mean	46.9		46.9	
S.D	12.1		12.0	

The distribution of breast cancer cases according to clinical stage is given in Figure 1.

Figure 1. Percentage of Cases According to the Stage of Cancer



Educational attainment shows that all women were graduated from schools under university levels (see Table 2). Women graduated from senior high school were at smaller risk for breast cancer (RR= 0.41 ; 95% CI = 0.2 - 0.87).

Table 2. Relative risk of education among groups

Education	Case		Control		Rr	95 % Ci
	n	%	n	%		
Illiterate	78	26.0	149	24.8	0.59	0.28 - 1.24
Elementary	108	36.0	195	32.5	0.63	0.30 - 1.30
Junior.H.S	46	15.3	93	15.5	0.56	0.26 - 1.21
Senior.H.S	**53**	**17.7**	**146**	**24.4**	**0.41**	**0.20 - 0.87**
University	15	5.0	17	2.8	1.00	

Concerning the demographic origin, urban dwellers were at increased risk (RR= 2.22 ; 95% CI = 1.63 - 3.02), as can be seen in Table 3.

Table 3. Relative risk of geographical origin among groups

Geographic	Cases		Controls		Rr	95% Ci
	n	%	n	%		
Rural	105	35.0	117	29.5	1.0	
Urban	**195**	**65.0**	**482**	**70.5**	**2.22**	**1.63 - 3.02**
Total	300		599		899	

Table 4 shows relative risk by marital status. Breast cancer risk was significantly smaller among separated or widowed as compared to married women .

Table 4. Relative risk of marital status among groups

Marital Status	Case		Control		Rr	95% Ci
	n	%	n	%		
Married	197	65.7	331	55.2	1.0	
Seperated	**16**	**5.3**	**72**	**12.0**	**0.37**	**0.21 - 0.65**
Widowed	**64**	**21.3**	**157**	**26.2**	**0.68**	**0.49 - 0.96**
Unmarried	23	7.7	39	6.5	0.99	0.57 - 1.75
Total	300		599			

Breast trauma was proved to be a significant breast cancer risk factor (RR= 1.88; 95% CI = 1.09 - 3.25), as shown in table 5.

Table 5. Relative risk of breast trauma among groups

Trauma	Case		Control		Rr	95% Ci
	n	%	n	%		
Yes	**26**	**8.7**	**28**	**4.7**	**1.88**	**1.09 - 3.25**
No	271	90.3	549	91.5	1.0	
Total	297		577			

It was found that under-weight (Body mass index/BMI less than 17) was a significant risk factor (RR= 2.22; 95% CI= 1.22 - 3.96), but over-weight (BMI: 22 - 25) seemed to show protective effect (RR= 0.32 ; 95% CI = 0.22 - 0.45) as compared to normoweight (BMI : 17 - 21). See Table 6.

Table 6. Relative risk of body weight among groups

Body Weight (BMI)	Case		Control		Rr	95% Ci
	n	%	n	%		
Under-W.	**30**	**10.0**	**24**	**4.0**	**2.2**	**1.22 - 3.96**
Normo-W.	92	30.7	162	27.0	1.0	
Over- W.	**109**	**36.3**	**319**	**53.2**	**0.32**	**0.22 - 0.45**
Obese	67	22.3	90	15.0	1.31	0.87 - 1.97
TOTAL	298		595			

note : under.w : < 17 over.w : 22 - 25
normo.w : 17 - 21 obese : > 25

Tabel 7 shows that some irregular menstrual cycle might show protective effect (RR=0.08; 95% CI= 0.02 - 0.4).

Table 7. Relative risk of menstrual type among groups

Menstrual Regularity	Case		Control		Rr	95% Ci
	n	%	n	%		
Always reg	216	72.0	391	65.2	1.0	
Some irr	**84**	**28.0**	**209**	**34.8**	**0.73**	**0.54 - 0.98**
Total	300		600			

note: always regular : regularity for 3 period (< 20, between 20-30 and over 30 yrs)
sometime irregular : least 1 period irregularity

The food pattern analysis, revealed that vegetable diet was not a protective factor. But "Bad fatty diet " (consumed fatty meat, fatty food or coconut milk daily)

was significantly found as a risk factor for breast cancer (RR= 2.63, 95% CI= 1.45 - 4.79), as can be seen in Table 8 .

Table 8. Relative risk on diet fatty among groups

Fatty Diet	Case		Control		Rr	95% Ci
	n	%	n	%		
Good	111	37.0	257	42.8	1.0	
Average	164	54.0	321	53.5	1.18	0.88 - 1.58
Bad	**25**	**8.3**	**22**	**3.7**	**2.63**	**1.45 - 4.79**
Total	300		600			

note: good : consumed fatty meat, fatty food or coconut milk less than once a week.
average: consumed fatty meat, fatty food or coconut milk less than three times a week.
bad : consumed fatty meat, fatty food or coconut milk milk almost daily.

Experience of 1-2 pregnancy, was identified as a risk factor (RR= 1.51 , 95% CI= 1.02 - 2.23). Menopause and induced menopause were found to be a risk factor (RR 1.38, 95% CI= 1.04 - 1.84 and RR=5.96, 95% CI = 2.78 - 12.79). Breastfeeding or lactation for a very short term (less than 4 months) was found to be a risk factor (RR= 5.44, 95% CI= 1.88 - 15.75). See Tables 9, 10 and 11.

Table 9. Relative risk of pregnancy among groups

Pregnancy	Case		Control		Rr	95% Ci
	n	%	n	%		
None	40	13.3	81	13.5	1.02	0.66 - 1.59
1 - 2	**67**	**22.3**	**92**	**15.3**	**1.51**	**1.02 - 2.23**
3 - 4	79	26.3	197	32.8	0.83	0.59 - 1.18
> 5	109	36.3	226	37.7	1.0	
Total	295		596			

Table 10: Relative risk of menopausal status among groups

Menopause	Cases		Control		Rr	95 % ci
	n	%	n	%		
Not yet	135	45.0	329	54.8	1.0	
Naturally	**145**	**48.3**	**263**	**43.8**	**1.38**	**1.04 - 1.84**
Induced	**19**	**6.3**	**8**	**1.3**	**5.96**	**2.78 - 12.79**
Total	299		600			

Table 11. Relative risk of lactation among groups

Lactation	Case		Control		Rr	95% Ci
	n	%	n	%		
Never	49	16.3	94	15.7	1.14	0.78 - 1.67
Very short	**0**	**3.0**	**3**	**0.5**	**5.44**	**1.88 - 15.75**
Short	7	2.3	10	1.7	5.53	0.58 - 4.04
Average	15	5.0	18	6.0	1.82	0.91 - 3.65
Long	216	72.0	472	78.6	1.0	
Total	296		587			

note : very short : less than 4 mos
short : 4 - 6 mos
average : 7 - 24 mos
long : more than 24 mos

Contraception use and hormonal exposure by contraception, were found not to be a risk factors. Smoking habit was not also associated with breast cancer. But close genetic traits was an important risk factor (RR= 2.85, 95% CI= 1.41 - 5.74). See table 12.

Table 12. Relative risk of genetic trait among groups

Genetic	Case		Control		Rr	95% Ci
	n	%	n	%		
None	247	82.3	508	84.7	1.0	
Distant	35	11.7	79	13.2	0.91	0.60 - 1.40
Close	**18**	**6.0**	**13**	**2.1**	**2.85**	**1.41 - 5.74**
Total	300		600			

note :
distant : has malignancy case among family member such as father, brother, and other male family branches.
close : has malignancy case among family member such as grand-mother, mother, sister and other female family branches.

Table 13 shows that exposure to X-ray was identified as a significant protective factor (RR= 0.08, 95% CI= 0.02 0.4)

Table 13. Relative risk of x-ray exposure among groups

X-ray Exp	Case		Control		Rr	95% Ci
	n	%	n	%		
Never	46	15.3	91	15.2	1.0	
Indirectly	**1**	**0.3**	**25**	**4.2**	**0.08**	**0.02 - 0.4**
Direct	253	84.4	484	80.6	1.03	0.79 - 1.52
Total	300		600			

note:
never exposed : never experienced any radiological examinaion nor treatment.
indirectly exposed: ever experienced any radiological examination or treatment outside the chest region.
directly exposed : ever experienced any radiological examination or treatment at the chest region.

DISCUSSION

From the number of respondent, this study was one of the largest study on breast-cancer in Indonesia. One limitation of the study was that the controls were recruited only from the surgery department due to administration problem in the hospital.

The age of breast cancer cases in Indonesia was relatively younger than in Western countries and Japan.[4,5] Whether such finding was due to the fact that most of the respondents were from low socio-economic strata needs clarifying.

Breast trauma was significantly shown to increase the breast cancer risk. It is of interest, since trauma has never been reported as one of risk factors, so far. Unfortunately, the type and nature of the breast trauma was unable to be described in more details.

Early menarche and late menopause have been reported to be significant risk factors for breast cancer by others. [4,8] Our data did not confirm their findings. But, naturally menopause and induced menopause significantly increased the breast cancer risk.

Late first pregnancy has been also associated with increase of risk of breast cancer.[4,5] Such finding was not obtained in our study. On the other hand, this study showed that experience of low number (one to two) of pregnancy provided a slight increased risk of breast cancer. This was in agreement with other reports.
Whether hormonal contraception exposure was related to increased risk of breast cancer remains intriguing. Our data did not show such relationship, which is similar to other related studies.[4,9-11]

Several studies has revealed the association between the preventive effect of prolonged breastfeeding or lactation with breast cancer.[12-15] Our study provided such an evidence, where a woman who performed breastfeeding less than 4 months (very short duration of lactation) has 5 times higher risk to develop breast cancer.

History of breast cancer in the family, especially on the mother side has been reported as a strong risk factor.[4,16] In our study, close genetic relationship from mother side was significantly shown as a risk factor.

Body weight has a special relationship with breast cancer. Some studies indicated that obesity was related to increase the risk of breast cancer.[4,8,16-18] Our study also found that over weight was associated with a slight increased risk of breast cancer, while obese was not. Under nutrition was also found to be a risk factor.

The present study was also aimed to analyze whether diet has a special influence on the risk for breast cancer. Similar to other reported studies we found that "bad diet" which relate to the intake of the fat in the diet increased significantly the risk of breast cancer.[4,5] This finding has been very interesting, since the earlier studies did not obtain significant results.[16,19,20] Actually, the general consumption of meat, milk and canned food by the Indonesian people have been considerably low. But, some ethnic groups incorporated coconut milk in their daily food, both for cooking the main dishes and desserts or snacks. Thus the data showed that fatty meat, coconut milk , whole milk and canned food were the kinds of food items related to the bad fatty diet.

Smoking and drinking in our study, were not significant risk factor. In the old generation, this two habits were not popular.

The x-ray exposure data could not be interpreted and might be insufficient.

Beside the increasing effect of breast cancer risk of the above mentioned factors, separated and widowed marital status has a reducing effect. Not many studies explaining this phenomena, but stress related to marital situation might be conceivable to such an effect.

As a conclusion of this study, we found that the most prominent risk factors were induced menopause and short term breastfeeding or lactation i.e. less than 4 months (RR: 5.96 & 5.44 respectively). The risk of getting breast cancer was two to three times increased in patients with under-weight, close genetic traits and fatty diet (RR: 2.2 ; 2.85 and 2.63 respectively). The

relationship of hormonal contraceptive with the risk of breast cancer was not shown in this study. Since fatty food was found as one of the important risk factors, further study has been extended with further nutritional analysis.

Acknowledgments

The authors are grateful to the nurses, Ms. Ros and Emi, and public health nurses, Ms. July and Ms. Erlaini for excellent epidemiological data collection. We are also indebted to EDP staffs for helping in data processing.

This work was supported by the Ministry of Education and Culture, Japan, Grants No. 01042007 and 04042013; and was partly supported by the Indonesian Cancer Foundation. This collaborative study was a part of Special Cancer Research Project in Monbusho International Scientific Research Program, with the approval of the Dean, faculty of Medicine, University of Indonesia, No. 4383 / PT02.H4.FK / E / 88.

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