Histopathological aspects of breast cancer in relation to some epidemiological risk factors

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Abstrak

Penelitian epidemiologik dengan cara kasus kontrol pada 300 kasus kanker payudara di Rumah Sakit Dr. Cipto Mangunkusumo, telah dilakukan pada tahun 1989-1991. Dengan menggunakan klasifikasi yang dianjurkan oleh Japanese Breast Cancer Society, *gambaran histopatologik kanker payudara menunjukkan bahwa dari tipe karsinoma duktus invasif, jenis skirus ditemukan pada 147 kasus (49%), jenis padat tubuler pada 79 kasus (26.33%) dan jenis pa pilotubuler pada 39 kasus (*13%*). Sedang dengan menggunakan klasifikasi WHO (1981), ditemukan 265 kasus (88.33%) invasif duktus karsinoma, karsinoma invasif lobuler pada 7 kasus (2.33%), karsinoma moduler pada 17 kasus (5.68%), karsinoma adenoid kistik pada 1 kasus (0.33%), penyakit Paget pada puting 2 kasus (0.67%) dan 4 kasus pada karsinoma noninvasif adalah karsinoma duktal insitu. Analisa terhadap faktor-faktor risiko yang bermakna pada kanker payudara wanita Indonesia menunjukkan bahwa faktor-faktor: aktivitas seksual dini, tinggal di daerah perkotaan, trauma payudara, obesitas (kegemukan), haid pertama/menarche yang terlambat, siklus haid yang tidak teratur, menopause, konsumsi makanan berlemak dan yang mengandung santan dapat meningkatkan risiko. Juga telah dianalisa hubungan antara faktor-faktor risiko yang bermakna tersebut dengan jenis histopatologik. Hasilnya menunjukkan bahwa Konsumsi makanan bersantan meningkatkan kemungkinan jenis karsinoma duktus invasif. Pengaruh tersebut berhubungan dengan ketiga subtipe histologik, yaitu papiler tubuler; solid tubuler dan skirus. Konsumsi minuman dengan santan/air kelapa dan sayuran segar menurunkan kemungkinan jenis tersebut, dengan sifat tidak bergantung kepada subtipe histologik.*

Abstract

Case control epidemiological study of 300 breast cancer cases from Dr. Cipro Mangunkusumo Hospital has been performed in 1989-1991. By applying the Japanese Breast Cancer Society classification, the histopathological pattern of breast cancer showed that from the invasive ductal carcinoma type, scirrhous type was found in 147 cases (49%), solid-tubular type in 79 cases (26.33%) and papilotubular type in 39 cases (13%). According to WHO classification (1981); they were diagnosed as: invasive ductal carcinoma in 265 cases (88.33%), invasive lobular carcinoma in 7 cases (2.33%), medullary carcinoma in 17 cases (5.68%), adenoid cystic carcinoma in 1 case (0.33%), pure Paget's disease of the nipple in 2 cases (0.67%) and 4 cases (1.33%) of the noninvasive carcinoma were ductal carcinoma in situ. Analysis of the significant risk factors among the Indonesian female breast cancer revealed that thefollowing factors: living at urban area, young sexual activity, trauma, obesity, late menarche, irregular cycle, menopause, fatty diet and coconut milk containing food consumption increased the risk. Relationship of the risk factors to histopathological types has been stastistically analyzed. The results showed that increased possibility to have the invasive ductal carcinoma was related to consumption of coconut milk containing food. The effect was related to the three histological subtypes, namely: papillary tubular, solid tubular and scirrhous types. Coconut milk drinks and fresh vegetables showed decreasing effect, which was irrespective to subtypes.

Keywords: *Breast cancer, histopathological, epidemiological, risk factors .*

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INTRODUCTION

Breast cancers have a large variation of histological type.1 2 And the WHO classification was generally accepted to be used as a standard criterion on histological typing of whole body tumors. According to the WHO histological typing of breast cancer,3 there are 3 main groups of breast cancer: noninvasive carcinoma (DCIS, LCIS), invasive carcinoma (11 variants, inclusive IDC-, LC-papillary carcinoma and the others/special type carcinoma as usually mention in some modification of breast cancer classification),

Paget's disease of the nipple. In 1986, the Japanese Breast Cancer Society suggested to observe more carefully on the most common invasive breast carcinoma: IDC. As the result of their study, there are 3 subtypes of the IDC which were easily identified by light microscopic examination, namely: Papilotubular IDC, Solidtubular IDC, and Scirrhous IDC. These 3 subtypes of IDC have 10 years survival rate of 77.4%, 64.9% and 61.2% respectively.4

Age influences on some breast cancer types in relation to prognostic decision. For example: lobular carcinoma tubular carcinoma, Paget's disease, usually found on an elder age, ductal carcinoma on reproductive period in women and on an elder age in men, Junevile secretory carcinoma on childhood, mucinous carcinoma among the 5th decade, medullary carcinoma in the lower decade. In general, it was known that some breast cancer types have a specific biologic behavior: indolent, circumscribe or aggressive, diffuse/massive invasive.5-12

Some difference on histological type might be found among different races. In comparative study between Japanese and American female breast cancer, it was revealed that lobular carcinoma among Japanese females was significantly lower than that among American females. The Japanese breast cancer cases had better survival compared to the American cases.5

Race factor was established by some epidemiological observer5-9: white people-women have the highest risk of suffering breast cancer and medullary carcinoma was reported more frequently among the black.

In this paper, we present the analysis on the relationship between certain histological types of breast cancer to certain demographic characteristics and risk factors.

MATERIALS AND METHODS

Collaborative tudy on etiology and clinicopathology of breasl cancer on the first three years (1989-1990) using 300 case of breat cancer and 2 matched controls population at Dr. Cipto Mangunkusumo Hospital. Several results have been presented on One Day Symposium in International Collaborative Study on Breast Cancer at Jakarta, in 1993.

Based on Tjahjadi et al.13 and Setyawati et al.14 data, it will be studied whether histopathoJogical types of breast cancer showed any relati on to some epidemiological data. The result of case distribution by histological types was as follows: noninvasive ductal carcinoma (DCIS) 4 cases (1.33%), invasive ductal carcinoma (IDC) 265 cases (88.33%), consisting of 3 subtypes papilotubular IDC 39 cases (13%), solid-tubular IDC 79 cases (26.33%), scirrbous IDC 147 cases (49%), mucinous carcinoma 6 cases (1.33%), medullary carcinoma 17 cases (5.68%), invasive lobular carcinoma (JLC) 7 cases (2.33%), adenoid cystic carcinoma lca e (0.33%) and Paget's disease of the nipple 2 cases (0.67%).

The most frequent carcinoma: IDC (88.33%), conisted of scirrhous type 49% (the most frequent carcinoma IDC subtype). Looking at the age distribution table breast cancer in you ng people was relatively rare. Cases under 30 years old were found only in 13 cases (4.33%).

The distribution according to tumor location showed that tumors were mostly located at the left breast 172 cases (57.33%), followed by right breast 117 (39%) and 11 cases (3.67%) were bilateral.

The epidemiological study on the 300 cases of breast cancer revealed several significant risk factors, listed as urbaner, young first sexual contact, trauma, obesity, late menarche, irregular cycle, coconut milk food, no vegetable, and as significant at 1% menopau e and fatty diet. Among 17 histological types, 3 most frequent invasive carcinoma; papillary tubular, olid tubular and scirhhous types belonging to invasive ductal carcinoma were analyzed in relation to certain risk factors. Thus, living area, menopausal status, consumption of coconut milk containing food and drinks, and vegetables were evaluated against the relationship to invasive ductal carcinoma as compared to other types. They were further evaluated against the three histological subtypes. The proportions were compared by chi-square calculation with correction for continuity.16 Test for trend was performed using loglinear regression model with Poisson error.15

RESULTS

Basic results of our 300 cases breast cancer study presented in the following tables.

The most common histological type was the invasive ductal carcinoma (IDC): 88.33% followed by the peciaJ types: 9.67%, and the non-invasive carcinoma of ductal type (DCIS): 1.33%, Paget's disease of the nipple: 0.67%.

Table 1. Histological types and case distribution of breast cancer (1989-1991)

Histological types	Number of cases	%
1. Noninvasive carcinoma		
- Ductal	4	1.33
- Lobular	0	0.00
2. Invasive carcinoma		
a. Invasive ductal carcinoma		
a.I. Papilotubular	39	13.00
a.2. Solid-tubular	79	26.33
a.3. Scirrhous	147	49.00
b. Special type		
b.1. Mucinous	6	1.33
b.2. Medullary	17	5.68
b.3. Invasive lobular	7	2.33
b.4. Adenoid cystic		0.33
3. Pagets disease	2	0.67
Total	300	100.00

Source: Tjahjadi et al. 1993

Table 2. Case distribution by age at operation/biopsy

Age at operation/biopsy	Number of cases	%
20 - 29 years	13	4.33
30 - 39 years	72	24.00
40 - 49 years	93	31.00
50 - 59 years	55	18.33
60 - 69 years	58	19.33
70 - 79 years	9	3.00
Total	300	100.00

The peak incidence was found in the 5th decade: 31%. The youngest case reported was 21 years old, and the oldest case was 75 years old. The young people group (less than 30 years old) showed much lower percentage in comparison to the older people group (more than 40 years old), they were 4.33% versus 77.66%. The mucinous carcinoma which were only 4 cases (1.33%) occurring at 30 years, 44 years, 51 years and 54 years old respectively. The lobular and medullary types were similarly distributed in the age interval over 20 to 70 years. Among our 11 bilateral breast cancer cases, only 2 cases of them were lobular type.

The possibility of any kind of relationship between the histopathological types of the 300 cases of breast cancer and significant risk factors was analyzed by cross tabulation. The invasive ductal carcinoma

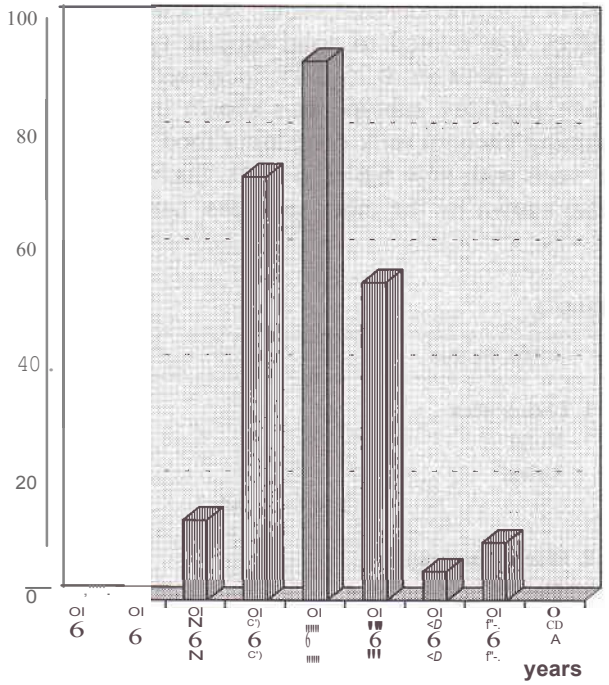

Figure 1. Histogram offrequency distribution by age of group of 300 cases of breast cancer

(IDC) type was analyzed in relation to living area, menopausal status, consumption of coconut milk containing food and drinks, fatty meat and fresh vegetables. The results are given in Table 3. There was no significant or difference in relation to IDC type or IDC type comparing between rural and urban area, with $x2 = 0.009$. Similarly, if they were compared according to menopausal status, with $x2 = 0.400$.

Consumption of coconut milk food seemed to increase the possibility to have invasive ductal carcinoma compared to other types. Significant difference was shown by women who consumed coconut milk food less than once a week, with $x2 = 5.885$, $p < 0.02$. Somewhat similar pattern was shown by consumption of coconut milk drinks, except for significantly decreasing effect related to frequent consumption (3-4 times weekly), with $x2 = 4.731$, $p < 0.05$. Consuming fresh vegetables daily showed to decrease the risk significantly. Further analysis was performed by evaluating the three subtypes of IDC, namely papillary tubular type, solid tubular type and scirrhous type. The results are given in Table 4.

Accordingly, there was no significant difference among three histological subtypes in relation to living area. However, there was marginal significance in

relation to menopausal status. Somewhat increasing effect was related to solid tubular type with x2 = 3.786, p between 0.25-0.05. Increased possibility to have papi llary subtype was shown in women consuming coconut milk containing food less than once a week with x2 = 6.685, p<0.01. Such an effect was also shown by the other subtypes, namely: solid tubular type with x2 = 4.014, p<0.05 and scirrhous type with x2 = 4.857, p<0.05. The tests for trend were not significant at p level of 0.05. No significant difference was seen for coconut milk drinks, fatty meat and fresh vegetables consumption relative to respective histological subtypes.

Table 3.

Risk factors	Invasive Ductal Carcinoma	Others	Total	x2	p
1. Living area					
Rural	93	12	105		
Urban	172	23	195	0.009	
Test for trend: 2. 0.001, p = NS					
2. Menopausal status					
No	118	17	135		
Yes	147	18	165	0.400	
Test for trend: 0.02, p = NS					
3. Diet of coconut milk containing food					
Never	61	12	73		
Less than 1x weekly	92	6	98	5.885*	< 0.02
1-2 weekly	57	7	64	1.382	
3-4 weekly	39	5	44	1.052	
Daily	18	3	21	0.331	
Test for trend: 0.007, p = NS					
4. Diet of coconut milk drink					
Never	159	25	184		
Less than 1x weekJy	80	6	86	3.212	
1-2 weekly	15	3	18	0.000	
3-4 weekly	10	6	11	4.731*	< 0.05
Daily				0.204	
Test for trend: 0.08, p = NS					
5. Diet of fatty meat					
Never	79	7	86		
Less than 1x weekly	80	15	95	1.809	
1-2 weekly	67	10	77	0.569	
3-4 weekly	33	3	36	0.106	
Daily	6	0	6	2.320	
Test for trend: 0.007, p = NS					
6. Diet of fresh vegetable					
Never	53	10	63		
Less than 1x weekly	42	6	48	0.599	
1-2 weekly	46	10	56	0.002	
3-4 Daily	57	5	62	2.619	
Daily	67	4	71	4.915*	< 0.05
Test for trend: 0.48, p = NS					

* *the two-sided significant level was determined*

Tabel 4. Analysis of risk factors and histological type of 300 breast cancer cases

Risk factors	Histological type						Others	Total
	Papillary tu bular roe	x2	Solid tub. roe	x2	Scirrhous roe	x2		
1. Living area								
Rural	18		23		52		12	105
Urban	21	0.642	56	0.596	95	0.006	23	195
2. Menopausal status								
No	19		27		72		18	135
Yes	20	0.217	52	3.786	75	0.201	17	165
3. Diet of coconut milk containing food								
Never	6		21		34		12	73
Less than Ix weekl y	14	6.685**	28	4.014*	48	4.857*	6	98
1-2 weekly	12	4.593*	17	0.729	28	0.819	7	64
3-4 weekly	5	1.610	10	0.280	24	1.379	5	44
Dail y	2	0.652	3	0.301	13	1.863	3	21
Testfor trend:		*0.222*		*1.341*		*0.612*		
4. Diet of coconut milk drink								
Never	28		46		85		25	184
Less than Ix weekl y	9	0.617	25	3.368	46	3.625	6	86
1-2 weekly		0.308	5	0.068	9	0.038	3	18
3-4 weekly	1	2.297	3	2.136	6	2.929	6	11
Dail y	0	0.001	0	0.085		0.004		
Testfor trend:		*1.813*		*0.091*		*0.708*		
5. Diet of fatty meat								
Never	11		29		39		7	86
Less than lx weekly	11	0.846	21	3.207	48	0.675	15	95
1-2 weekly	LO	0.130	20	1.004	37	0.238	10	77
3-4 weekly	6	0.469	8	0.018	19	0.290	3	36
Dail y		3.421		3.182	4	2.536	0	6
Testfor trend:		*0.273*		*1.437*		*0.416*		
6. Diet of fresh vegetable								
Never	9		18		39		10	63
Less than 1x weekly	5	0.077	14	0.525	48	2.475	6	48
1-2 weekly	9	0.105	13	0.077	37	0.021	10	56
3-4 weekly	8	1.321	15	1.222	34	1.502	5	62
Dail y	8	2.022	19	3.148	40	3.291	4	71
Testfor trend:		*0.101*		*0.142*		*2.383*		

* *Significant difference at p<0.05;* ** *Significant difference at p<0.01*

DISCUSSION

The age distribution of the Indonesian female breast cancer showed that a significant increase of the proportion of cases has started at the third decade (24%) and peaked at the fourth decade (31%). The data suggested that the breast cancer in Indonesian females started at younger ages compared to the American and the Japanese cases.5-13 The proportion sharply declined at the seventh decade, similar to the Japanese cases but differs from the American cases, which declined at the eighth decade.

The histological typing showed that the majority was the invasive carcinoma (98%), consisting of 88.33%

invasive ductal carcinoma and 9.67% special type. Thus, only a few non-invasive carcinoma (l.33%) and Paget's disease of the nipple (0.67%). The proportion were different from the Japanese cases,5-13 with higher non-invasive cases (7.4%), lower invasive ductal carcinoma (80.4%), lower special types (11.4%) and similar Paget's disease (0.7%). The present study has analyzed the relationship between several significant risk factors and the histological types. The data showed that consumption of coconut milk containing food increased the possibility to have invasive ductal carcinoma as compared to other histological types, while coconut milk containing drinks and fresh vegetables had decreasing effect. It is of interest that the increasing effect of coconut milk containing food related to papillary tubular type and the decreasing effect of coconut milk containing drinks was related to scirrhous type. It appeared that the former effect was evident in all three histological subtypes. The decreasing effect of fresh vegetables was not preferentially related to any histological subtype. Such relationship might be value for better understanding on the role of risk factors in influencing the development of breast cancer. The relationship of histological types of gastric cancer to demographic data has been also analyzed by others.17

Further study on bigger samples is suggested to enable the analysis on other histological types and the evaluation on important epidemiological risk factors such as ethnic difference.

Acknowledgments

The authors would like to thank 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, Science, Sports and Culture of Japanese Government, Grants No. 01042007, 04042013 and 06042006; and was partially 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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