

Clinicopathology profile evaluated against several risk factors in breast cancer cases

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Abstrak

Telah dilakukan penelitian dua ratus dua puluh enam kasus kanker payudara (KPD) yang berhubungan dengan aspek klinik dan patologi serta faktor risiko yang berhubungan dengan terjadinya keganasan payudara. Distribusi terbanyak pada umur antara 35-55 tahun dengan frekuensi tertinggi antara umur 40-50 tahun. Tidak didapatkan perbedaan lokasi tumor pada payudara kanan atau kiri serta distribusi pre-menopause maupun post-menopause. Delapan puluh satu koma enam persen KPD ditemukan pada stadium lanjut (stadium IIA: 17,7%, IIB: 56,2% dan IV: 11,9%), sedangkan stadium I: 1,3% dan stadium II: 11,9%. Tujuh puluh Lima dari 226 kasus dilakukan tindakan pembedahan: 60% mastektomi simpel, 26,7% mastektomi radikal dan 1,3%: **breast cancer conserving treatment (BCT)**. Histopatologi dari jaringan payudara dari 214 kasus didapatkan karsinoma invasif yang terdiri dari: 90,4% karsinoma duktal invasif dan 9,6% tipe khusus. Dilakukan analisa dari beberapa faktor risiko seperti status kawin, umur pada saat kawin pertama, umur menarche, status menopause, laktasi, riwayat keluarga KPD, penggunaan kontrasepsi dan konsumsi tinggi lemak. Hasil dari metode kasus kontrol menunjukkan bahwa faktor-faktor status menopause, laktasi dan konsumsi tinggi lemak meningkatkan risiko terjadinya KPD, dengan risiko relatif masing-masing: 1,51, 1,83 dan 2,61.

Abstract

The second batch case-control study on breast cancer has been conducted as a joint study between Indonesian and Japan. Two hundred and twenty six (226) cases of breast cancer was collected to assess the risk factors and evaluated for their clinical presentation of the disease. The age distribution in some high risk areas showed at age 35 to 55 years, with a single peak between 40 to 50. There was no difference in number of cases in respect to tumor site and menopausal status. The majority of cases 81.6 % were in advanced stage (IIA: 17.7%, IIB: 56.2% and IV: 11.9%) while in contrast stage I and II were very rare (1.3% and 11.9% respectively). Only 75 cases were operable; simple mastectomy was the most frequent surgery carried out (60.0%), followed by modified radical mastectomy (26.7%), classical radical mastectomy (12%) and breast conserving treatment (1.3%). The specimens were reviewed using classification recommended by the Japanese Breast Cancer Society revealed invasive ductal carcinoma (90.4 o/o) and the special type (9.6 o/o). Several risk factors were analyzed for their influence to the development of breast cancer; namely: marital status, age at first marriage, menarche, menopausal status, lactation, family history of breast cancer; use of contraceptive and fat consumption. Among the characteristics studied, the following factors significantly increased the risk of breast cancer: menopausal status (RR= 1.51; 95% CI: 1.10-2.09), non-lactating children (RR=1.83; 95% CI: 1.07-3.11) and fat consumption (RR=2.61; 95% CI: 1.86-3.68), while the use of contraceptive showed protective effect. The findings will be discussed in its benefit relative to both the improvement of the treatment modality and the cancer control program.

Keywords: Breast cancer, clinicopathological, case-control study, epidemiology

INTRODUCTION

Carcinoma of the breast continue to baffle the surgeons and the pathologists for the unpredictable biological behavior and many gap in the knowledge of the factors that either control or influence tumor genesis and growth. In Indonesia breast cancer ranked second most common malignant tumor of the females. Up to 678 cases of breast cancer were hospitalized in Dr. Cipto Mangunkusumo Hospital, Jakarta, during the 5 years period- 1986-1990. Data collected from Pathological Base Cancer Registry showed relative frequency 18.03% with Age Stand-

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ardize Cancer Ratio (ASCAR) 17.84% in 1988 and 18.44% (ASCAR 17.48%) in 1989.¹

More articles have been published on breast cancer.²⁻⁷ but accumulation of knowledge has not produce any commensurate degree of agreement among research worker and clinicians on epidemiological, etiological, pathological and treatment problem of breast cancer. Thomas Huxley wrote "A great tragedy of science - the staying of a beautiful hypothesis by an ugly fact". Wider understanding of different modalities, natural history of the disease and host-tumor relationship are some of the encouraging factors toward better salvage of this disease. A team work is needed for the management of breast cancer without prejudice to the specialty.

This study was conducted to find out the clinico-pathological findings and incidence of the disease in relation to other parameters along with the known etiological factors.

MATERIAL AND METHODS

Material s consisted of women who underwent treatment at the Division of Surgical Oncology, Department of Surgery - Dr. Cipto Mangunkusumo Hospital, Jakarta, during the period of February 1992 to September 1995 and were diagnosed as having histologically confirmed breast carcinoma. The medical records comprising 226 cases, aged 29 to 74 years (median age 45 years), were reviewed. A detailed clinical history and clinical examination were taken. Clinical staging was done by criteria according to the International UICC TNM System for Malignant Tumors and the surgical specimens were reviewed using the classification recommended by the Japanese Breast Cancer Society (1984)⁹.

With the same cases (226) several potential factors for breast carcinoma, namely: marital status, age at first marriage, menarche, menopausal status, lactation, family history of breast cancer, use of contraceptive and fat consumption were recorded. A case-control study design with 1:2 ratio was applied in this assessment. Each risk factor was assessed through univariate analysis and was measured its estimated Relative Risk and 95% Confidence Intervals.

RESULTS

Age

We found that significant increase of the proportion

of breast cancer cases in women started and peaked at comparatively younger age as compared to women in the Western countries. Table 1 and Figure 1 shows the details of age incidence and the commonest incidence was in age groups 30-39, 40-49 and 50-59 (28.3%, 30.1 % and 28.8%) respectively. The incidence sharply decrease with advancing age. The youngest case of breast cancer was 29 years old and the oldest 74 years.

Table 1. Distribution of 226 cases of breast cancer and 552 controls according to age of patients

Age	Cases	%	Control	%
25 - 29	3	1.3	4	0.9
30 - 39	64	28.3	136	30.1
40 - 49	68	30.1	141	31.2
50 - 59	65	28.8	115	25.4
60 - 69	23	10.2	53	11.7
.....70	3	1.3	3	0.7
Total	226		552	

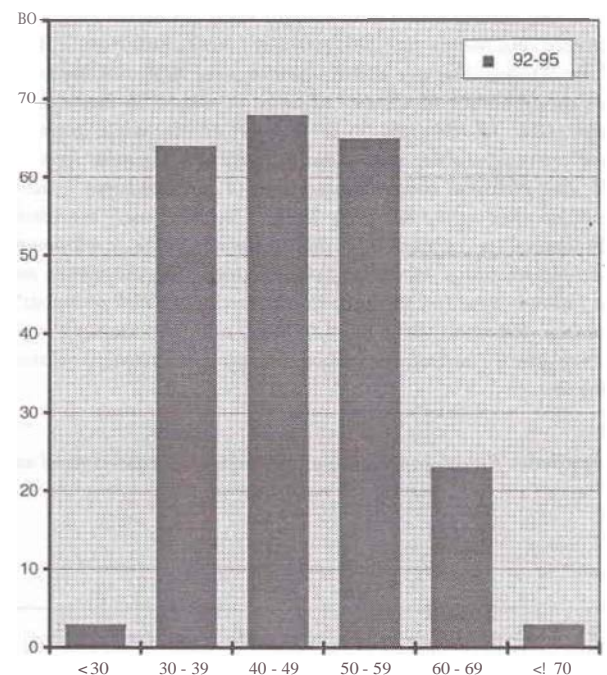


Figure 1. Age distribution of 226 cases of breast cancer (histogram)

Menopausal status

Correlation with hormonal status is shown in Figure 2. One hundred thirteen (50.22%) cases were premenopausal and 112 (49.78%) were postmenopausal.

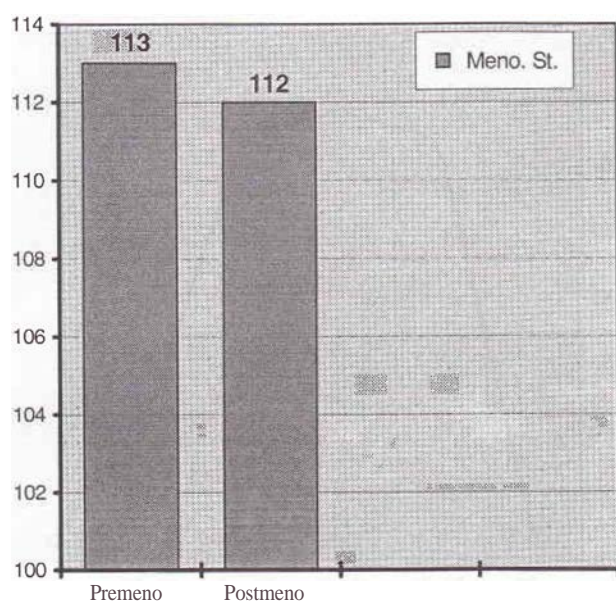


Figure 2. Distribution of 225 breast cancer by menopausal status

Clinical features

The right breast was involved in 48.2%, left breast in 48.7% and bilateral tumor was present in 1.8% (Table 2). Staging of the disease (Table 3) was done by the UICC TNM Classification of Malignant Tumors criteria; 1.3% were in stage I, 11.9% in stage II, 17.7% in stage IIIA, 56.2% in stage IIIB and 11.9% in stage IV. The highest number of cases had advanced disease (Stage IIIB) and proposed treatment was palliation.

Table 2. Side involvement of breast cancer cases

Side affected	No. of cases	%
Right	109	48.2
Left	110	48.7
Bilateral	4	1.8

Table 3. Distribution of breast cancer cases according to clinical staging (n = 226)

Stage	Cases	%
I	3	1.3
II	27	11.9
IIIA	40	17.7
IIIB	127	56.2
IV	27	11.9
Unknown	2	0.8
Total	226	100.0

Treatment

The treatment modality in operable cases (33.2%) is shown in Table 4. Radical mastectomy and modified radical mastectomy were adopted as initial treatment in the Department of Surgery for Stage I and Stage II which was done in 29 cases. Adjuvant radiation was performed if there was clinical evidence of regional metastasis. Stage IHA cases were treated by simple mastectomy (60%).

Table 4. Type of operation performed in 75 cases

Type of operation	No. of cases	%
Radical mastectomy	9	12.0
Modified radical mastectomy	20	26.7
Simple mastectomy	45	60.0
Lumpectomy	1	1.3

Histopathology

Histology classification of Japanese Breast Cancer Society have been adopted to classify breast carcinoma (Table 5). Scirrhus adenocarcinoma was the commonest type of cancer.

Table 5. Histological pattern of breast cancer cases according to classification recommended by Japanese Breast Cancer Society (1984)

Histological types	No. of cases	Right	Left	%
Non-invasive carcinoma				
Invasive carcinoma				
a. Invasive ductal carcinoma				
a1. Papillotubular	15	7	8	
a2. Solid-tubular	65	27	38	
a3. Scirrhus	118	61	57	
b. Special types				
b1. Mucinous carcinoma	5	4	1	
b2. Medullary carcinoma	10	5	5	
b3. Invasive lobular carcinoma	5	2	3	
b4. Squamous cell carcinoma				
c. Unclassified and other				
	11			
	225	106	113	

Notes: four cases bilateral

Table 6. Univariate logistic analysis of odds ratios (RR) and confidence interval (CI) for breast cancer risk factors

Covariates	Cases	Controls	RR	95% CI
Menarche				
< 15	109	232	1.00	Reference
15	116	218	1.13	(0.82-1.56)
Menopausal status				
No	112	270	1.00	Reference
Yes	113	180	1.51	(1.10-2.09)*
Marital status				
Married	177	354	1.00	Reference
Widowed	45	97	0.4	(0.62-1.40)
Unmarried	2	0		
Use of contraception				
No	170	311	1.00	Reference
Yes	49	133	0.67	(0.46-0.98)*
Lactation				
Yes	194	418	1.00	Reference
No	28	33	1.83	(1.07-3.11)*
Family BC				
No	213	422	1.00	Reference
Yes	6	22	0.50	(0.22-1.35)
Age of marriage				
20 yrs	98	222	1.00	Reference
< 20 yrs	121	222	0.81	(0.59-1.12)
Fat consumpt.				
≤ 26	65	232	1.00	Reference
> 26	161	220	2.61	(1.86-3.68)*
Calories intake				
≤ 1854	115	258	1.00	Reference
> 1854	111	194	1.28	(0.93-1.77)

DISCUSSION

Although the risk of breast cancer increases with progressing age,²⁻⁴ a special age curve distribution has been observed. From 226 cases (Fig: 3), breast cancer incidence rises quickly between ages 30 and 35, and levels on and off to a plateau between 35 and 55, and after age 55 decline slowly. This is different from De Waard's report (1964) of double peaks at 45 to 49 and 65 to 70. Henningsen (1975) reported only single peak between 50 and 60.4 Other dissimilar figure was incidence of breast cancer in young women, defined as 40 years or less. Commission on Cancer of the American College of Surgeons reported 23,974 cases diagnosed in 1990: 0.8% were 30 years of age or less and 6.6% were in the age range of 31 to 40. In the present study 1.3% were less 30 years and 28.3% in the age range of 30 to 39 years.

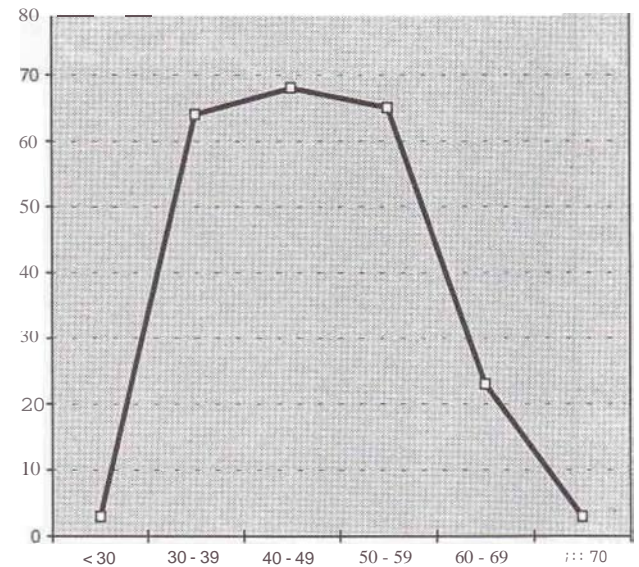


Figure 3. Age distribution curve for 226 breast cancer patients

The majority (85.8%) of 226 breast cancer were in advanced stage (IIIA, IIIB and IV) and 13.2% were in early stage. The present study were similar with previous data but different from breast cancer in Japan, 8-9 which the majority were in early stage. Only on 75 cases performed surgery and Simple mastectomy (60%) was mostly chosen procedure due to high portion of advanced stage (IIIA). Surgical modality in early cases were radical mastectomy (12%) and modified radical mastectomy (26.7%).

Ductal (scirrhous), solid-tubular, papillotubular, medullary, mucinous and invasive lobular carcinoma were diagnosed in 52.44%, 28.89%, 6.6%, 4.4%, 2.2% and 2.2% of cases, respectively. Consideration of the histological parameter, such as degree of tubular, gland formation, size of cells and nuclei (nuclear pleomorphism), degree of hyperchromatic and number of mitoses was also evaluated for prognostic evaluation. Sub type of invasive ductal carcinoma reflect the degree of differentiation such as well differentiated, moderate and poor differentiated in an order of papillotubular carcinoma, solid tubular carcinoma and scirrhous carcinoma. Depending on a grading system considering the above mentioned parameters, two third of the cases were grade III and only small portion grade I. The prognosis is usually favorable when tubular gland formation and stromal elastosis exist and when tumor mitosis and fibrosis are minimal (Wallgren et al, 1976).

Despite of clinical staging, histological type and grade of tumor had a role to predict prognosis of breast cancer.

This case control study has been conducted to confirm causal relationship of nine important determinant factors for the development breast cancer among Indonesian women (Table 6). Unlike women in the developed countries, the Indonesian women differ in many aspects such as familial, non familial (environments) and socio-economically. Nine determinant factors have been assessed using univariate analysis (Table 6), and three of them showed significant associations with the development of breast cancer, namely: menopausal status (RR=1.51; 95% CI: 1.10-2.09), lactation (RR=1.83; 95% CI: 1.07-3.11) and fat consumption (RR=2.61; 95% CI: 1.86-3.68). Menarche and the use of contraceptive which are related to endocrine factors had not been found to be significant factor in this study. The earlier the age of menarche, with its associated earlier onset of "regular" menstrual cycles, the higher risk of breast cancer. The findings were not consistent with the notion that early menarche had been demonstrated as a risk factor in many studies. It is known that the interval from the menarche up to the establishment of regular menstrual cycle might be a better estimate for determining the risk for breast cancer rather than the age of menarche. Women with early menarche (age 12 or younger) and rapid establishment of regular cycles had an almost fourfold increased risk of breast cancer when compared with women with late menarche (age 13 or older) and long duration of irregular cycles.¹¹⁻¹²

The use of contraceptive showed protective effect in this study, which was different from the results of the first batch of study. The discrepancy might be due to small samples. Such unclear findings were also reported elsewhere, thus, further study is necessary to clarify the effect.

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