



CHARACTERISTICS OF BREAST CANCER PATIENTS IN RSUP HAJI ADAM MALIK MEDAN, INDONESIA

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Abstract - Introduction: Breast cancer has a high prevalence in both developing and developed countries due to years of increased morbidity and mortality. Based on Pathological Based Registration in Indonesia, KPD ranks first with a relative frequency of 18.6% and more than 80% of cases were found in advanced stage, where treatment efforts are difficult. This study aims to obtain general and specific characteristics of breast cancer patients in RSUP Haji Adam Malik, Medan. **Method:** This was observational study that conducted in RSUP Haji Adam Malik, Medan which involved all cases of breast cancer diagnosed histologically. Clinical information and demographic data for patients were retrieved from surgical wards and department of medical records. Data was entered and analyzed by SPSS software. **Results:** Based on the general characteristics, the majority of breast cancer patients were 33 samples aged 40-49 years (34.7%), 41 samples (43.2%) finished high school education, 65 samples (68.4%) unemployed, and 91 samples (95.8%) did not have a family history of breast cancer. Based on specific characteristics, the majority of breast cancer patients were in stage IIIB, with 42 samples (44.2%) with T4b tumor size totaling 50 samples (52.6%), stage N1 numbering 40 samples (42.1%), and metastasizing in the lung were 11 samples (40.7%) in stage IV. There were 68 samples (71.6%) diagnosed with IDC, 70 samples (73.7%) with negative status of ER, 67 samples (70.5%) with negative status of PR, 31 samples (32.6%) with positive values of her2, and 49 samples (51.6%) with positive status of ki-67. **Conclusions:** Most of breast cancers patients in RSUP Haji Adam Malik Medan were experienced by young age women who did not work and already in stage IIIB and IV.

Keywords- Breast cancer; sociodemographic; staging; histopathology; immunohistochemistry.

I. INTRODUCTION

Breast cancer has reached the highest number of new cases (43.3%) and its death percentage has reached 12.9% according to age controlled GLOBOCAN/IARC 2012 data.¹ Breast cancer was the fifth leading cause of all female cancer deaths (522,000 deaths) and the most common cause of cancer death among women in developing regions (324,000 deaths, 14.3 % of the total), and is now the second leading cause of cancer death in developed regions after lung cancer (198,000 deaths, 15.4 %).

In 2017, it was estimated that 252,710 new cases of invasive breast cancer were diagnosed among women, according to the American Cancer Society (ACS), and 63,410 additional cases of in situ breast cancer. Race and ethnicity were also correlated with the prevalence of breast cancer, with the highest mortality rate among black non-Hispanic groups, namely 29.5%, in addition to age characteristics.

Based on 2013 Basic Health Research data from Indonesia, the Yogyakarta Special Region had the highest prevalence of 2.4% of the population diagnosed with breast cancer. East Kalimantan was in second place with a prevalence of 1%, followed by Jakarta and Aceh Special Area provinces with the same prevalence of 0.8%. With an absolute estimation of about 2,682 patients, the prevalence of breast cancer in North Sumatra was 0.4 %.^{2,3}

According to statistics from the Surabaya Oncology Hospital's Research and Development Department on the breast cancer profile in 2014, about 31.34 % of patients were 41-50 years old and 51-60 years old; 41.65 % had university education; 53.61 % lived in Java Island; 69.69 % had no family cancer history; 57.31 % were housewives; (Indonesian Journal of Cancer, 2015). According to data from Prof. Dr. RD Kandou Manado, 40 % of the population aged 40-49 years was the largest distribution of breast cancer patients in 2013-2014; 61 % of high school education; 96 % of patients had histopathological characteristics of invasive ductal carcinoma and 63.6 % were in stage IV.⁴

Breast cancer has remained as one of the global health issues due to increased morbidity and mortality. Socio demographic variables such as old age, education, occupation and family background, are linked with the prevalence of breast cancer both globally and nationally, based on some of the epidemiological evidence already mentioned. The categories of histopathology and cancer stages offer a summary of the progression rate of breast cancer, such that several research have taken place both in Indonesia and abroad.⁵ We are therefore interested in understanding the characteristics of the RSUP Haji Adam Malik Medan breast cancer patients.

II. MATERIALS AND METHODS

This conservational study with a descriptive method was conducted in RSUP Haji Adam Malik Medan by taking medical records of breast cancer patients from 2014-2016. The samples of this study were histopathologically diagnosed of breast cancer patients.

The data was collected then processed and analyzed descriptively to present the frequency distribution based on the characteristics, namely age, education level, occupation, family history, stage, location of metastases, histopathological

and immunohistochemistry features of breast cancer patients in the RSUP Haji Adam Malik Medan.

III. RESULTS

From 874 breast cancer patients registered on January 1, 2014 to December 31, 2016, selected 95 cases of breast cancer included in the study. The general characteristics observed were age, educational history, and family history of suffering from cancer. Specific characteristics assessed were cancer stage and staging, location of metastases, histopathology, and immunohistochemistry results.

TABLE 1. Distribution of study samples based on general characteristics of cancer patients

General Characteristics of Breast Cancer Patients	Frequency (N)	Percentage (%)
Gender		
Female	95	100
Age		
<30	2	2.1
30 - 39	27	28.4
40 - 49	33	34.7
50 - 59	22	23.2
60 - 69	8	8.4
70 - 79	2	2.1
≥ 80	1	1.1
Level of education		
Uneducated	1	1.1
Primary School	23	24.2
Junior High School	13	13.7
High school	41	43.2
University	17	17.9
Family History		
Yes	4	4.2
No	91	95.8

Based on table 1, all breast cancer patients in RSUP Haji Adam Malik Medan from 2014-2016 were female, with the majority age of breast cancer patients were 40-49 years old (34.7%). From educational level, the highest population was high school group with total of 41 samples (43.2%) and most of the samples did not have a family history of breast cancer, 91 samples (95.8%) and only 4 samples had a family history (4.2%).

TABLE 2. Distribution of study samples based on the specific characteristics of cancer patients

Specific Characteristics of Breast Cancer Patients	Frequency (N)	Percentage (%)
Stadium		
I	2	2.1
IIA	1	1.1
IIIB	14	14.7
IIIA	6	6.3
IIIB	42	44.2
IIIC	3	3.2
IV	27	28.4
Metastatic Location		
Bone	6	22.2
Lungs	11	40.7
Liver	7	26
Multiple sites	3	11.1
Histopathology		
Ductal Carcinoma In Situ	1	1.1
Invasive Ductal Carcinoma	82	86.3
Invasive lobular carcinoma	8	8.4
Inflammatory Carcinoma	1	1.1
Mucinous Carcinoma	1	1.1
Tubular Carcinoma	2	2.1
Estrogen Receptor		
Positive	25	26.3
Negative	70	73.7
Progesterone Receptor		
Positive	28	29.5
Negative	67	70.5
HER2		
2 Positive	1	1.1

3 Positive	31	32.6
Negative	63	66.3
Ki-67		
Positive	49	51.6
Negative	46	48.4

Based on table 2, the majority of breast cancer patients at RSUP Haji Adam Malik Medan were in advanced stage, which was stage IIIB, around 42 samples (44.2%) and stage IV (28.4%) and majority metastasized in the lung. From the results of immunohistochemistry, most patients histopathologically diagnosed with breast cancer were invasive ductal carcinoma (71.6%) and the highest type was Her-2 positive.

IV. DISCUSSION

Women's breast cancer is also at the forefront of Indonesia's cancer incidence. The incidence of cancer in North Sumatra rose from 1.0 per cent in 2013 to 1.8 per cent based on Riskesdas data in 2018. However, there have been reports of breast cancer in men that were yet to be recorded. The absence of male subjects in this study could be due to the absence of male breast cancer patients in RSUP Haji Adam Malik from 2014-2016. The American Cancer Society has predicted that there will be 2,550 new cases in 2018 and 480 men will die from breast cancer in America. The average chance for male breast cancer is about 1:1000. (1: 8 with women). Age is the common risk factor associated with breast cancer in both men and women.⁶

Based on this report, the majority of patients with breast cancer in RSUP Haji Adam Malik Medan were 40-49 years of age (34.7 percent). This is because women in this age group were more aware and worried about the changes that occur to them. There were so many women who did not know the signs of breast cancer due to lack of knowledge, low levels of education and lack of adequate treatment from their families. In addition, many young adults (under 50 years of age) were currently using oral contraception and did not breast-feed. Both of these factors have been extensively researched because of there was connection with the prevalence of breast cancer. These findings were in line with the results of research by Rondonuwu et al (2016) regarding the profile of breast cancer in Prof. Dr. RD Kandou Manado Hospital from 2013-2014 which reported that the highest prevalence was in the 40-49 years old category as many as 61 cases (43 percent). This, however, contradicts findings in America that have stated that new cases of breast cancer rise with age. It was estimated that both in situ and invasive breast cancer in the United States were usually found between 50 and 69 years of age. This is due to many risk factors, such as the use of hormonal menopause medication involving estrogen and progesterin, pollution, obesity, etc.^{7,8}

The results of this analysis are consistent with Rondonuwu et al (2016) studies, in which the majority of the education distribution of 92 patients was high school (61 percent). In addition, the research of Rick and Merinjo (2017) found that 98 women were in high school in Arusha, Tanzania (37.8 percent). However, Shariff-Marco et al (2014) Neighbourhood and Breast Cancer Population Study (NABC) in the San Francisco Bay Area confirmed that out of 4,639 samples, 1,416 patients (32%) were at vocational or university level, while only 782 patients were at high school level (18 percent). The same was also observed in Liu et al. (2017) who reported that, based on 10 years of epidemiological trials in China, the majority of cases were in non-specific education patients (50.3 per cent; $P < 0.001$). Teenagers studying in the university (16-18 years of age) accounted for just 20 per cent of the overall number of teenagers in North Sumatra.^{9,10}

In certain cases, family history is the main risk factor for breast cancer. Women with one female in the family

who have breast cancer are twice as vulnerable to developing breast cancer, and women with 2 breast cancer relatives are 14 times more likely to develop breast cancer. Whereas only 4 patients reported to have a family history of breast cancer in this study. The family history collected in the medical record were mostly obtained by history taking, while the identification of genes, such as the science of Precision Medicine that is currently being established, can be very helpful in evaluating whether or not the patient and family have gene mutations.⁷

The findings of this study were consistent with research conducted by Rondonuwu et al (2016) in which the majority of patients diagnosed with stage IV breast cancer reported 96 cases (63.6 percent). According to research conducted by Verdial et al (2017), based on SEER statistics from 1973 to 2013, the highest rates were observed in localized and in-situ groups (stage 0, I, and II). According to NAACCR 2017 data, the highest percentage of staging distribution was also at the localized stage. This was attributed to the American people's early detection awareness of breast cancer, as with mammography. 5

Based on the cancer staging, the primary tumor in this study was found to have direct skin extension (edema/peau d'orange, ulceration, or satellite skin nodules). This was because the majority of patients had been referred so that they were already at an advanced stage (stage III and IV). The findings of this study were in line with Munck et al (2018), which showed a total of 14899 patients were mostly at the advanced stage (approximately 15 mm) (52.5 percent). Several other research, however, such as Saadatmand et al (2015), Song et al (2015), and Welch et al (2016), have shown that T1c (tumors greater than 1 cm but not greater than 1 cm) were the largest distribution.¹¹

Xiao et al (2018) estimated that 11,568 stage IV patients were diagnosed, 4,213 (36.4%) patients were identified with BCLM (Breast Cancer Lung Metastases) and 1214 (10.5%) patients were diagnosed with lung metastasis. The findings of this study were also in line with Chen et al (2017) that the demographics of patients with stage IV breast cancer were primarily metastasized to the lungs in older patients from the SEER population data (Surveillance, Epidemiology, and End Results) from 2010-2013 ($P < 0.001$).¹²

Several studies have found that neutrophils played a role in colonizing cells that initiate breast cancer in the lung. The Wculek and Malanchi research (2015) therefore concluded that changes in the presence of neutrophils in the tissue can affect a particular subset of disseminated cancer cells. CD11b + Ly6G + neutrophil cells accumulated in the lungs before the tissue was infiltrated by cancer cells (pre-metastatic lung), and their numbers increased during metastatic progression (metastatic lung).¹³

The initial metastases of the breast cancer by anatomical location, however, was the bone via the Batson vein plexus. Based on the 2013 NCCN Guidelines, bone scans have been performed in patients who have experienced localized bone pain or elevated alkaline phosphatase enzymes in stage I-III and must be performed when they have entered stage IIIA. Several studies have also shown that the most metastatic sites are in the bone. The difference in the results of this study was due to the high cost of bone scans, so that this examination was rarely performed on patients with breast cancer in RSUP Haji Adam Malik Medan, and if they had just metastasized, the clinical manifestations were not clear.^{12,13}

The majority of women with breast cancer in this study had invasive ductal carcinoma (86.3 percent). This is due to the supportive anatomical location that the IDC begins with the cells in the lactiferous ducts of the breast glands that exit through the duct walls and expand into the fat tissue of the

breast. Through the lymph system and bloodstream, cancer would spread to other organs. The findings of this study are consistent with research conducted by Liana and Lirauka (2012) that the most common histopathology at Arifin Achmad Hospital Pekanbaru was invasive ductal carcinoma (96.9 percent). The same findings were also obtained by the Rondonuwu et al (2016) study with a total of 147 cases (96 percent). The study by Chen et al (2016) also concluded that invasive ductal carcinoma (IDC) was the most frequent histopathology observed at all ages, including in the young, middle-aged and older. According to the American Cancer Society, 8 of the 10 invasive breast cancers is IDC.¹⁴

Based on the immunohistochemistry evaluation, the study was not compatible with Palmer et al (2017) research that positive ER status was obtained in the group of African-American women compared to negative ER status in both the diabetes and non-diabetes groups. According to Kantelhardt et al (2014), 352 female patients with breast cancer who had ER status at Addis Ababa University Hospital, Ethiopia, were only 35 per cent negative. It has been stated in previous studies that the majority of sub-Saharan Africa's ethnic groups were negative (Ly M et al., 2012). Excessive expression of estrogen receptor negativity in previous studies was attributed to the poor reliability of the laboratory requirements for tissue handling, the method of fixation used. Iqbal et al (2015) suggested that the majority of the research sample had a positive PR status. Study by Kantelhardt et al (2014) also suggested that 162 out of 224 patients with breast cancer (72 per cent) had a positive PR status. This is not in line with this study where negative PR results were obtained. This was due to the fact that the majority of breast cancer patients in the United States were diagnosed at an early stage, so that the results of the IHC test appear to be positive for hormonal receptors, whereas while negative ER and PR status (her2 enriched and basal-like) tend to be found in advanced breast cancers (ABC).¹⁵

Her2 is declared to be positive if the score is 3 positive. The majority of breast cancer patients in RSUP Haji Adam Malik Medan were positive from this study. The findings of this study were inconsistent with the Bessonova et al (2011) study, which showed that the majority of patients with the first tumor were negative in all ethnic groups ($P < 0.0001$). Study by Holowatyj et al (2016) also reports that there has been more negative status of her2 based on data from the California Cancer Registry. This was because the majority of patients in United states were diagnosed with Luminal A (ER +/her2-) and Luminal B (ER +/her2+) subtypes.^{16,17}

The findings from this study are consistent with the Abubakar et al research (2016), where 8088 patients studied by the Genetics and Epidemiology Division of the Institute of Cancer Research London had positive results with low strokes. Research by Yabar et al (2017) also reported that all 580 patients in three hospitals in Peru (Hospital Nacional Edgardo Rebagliatti Martins, Hospital Nacional Guillermo Almenara Irigoyen, Hospital Nacional Alberto Sabogal, Lima) and Instituto Nacional del Cancer, Montevideo, Uruguay had a positive ki-67 result with the following information: the ER- and ki-67 had high streaks (68%), ER + and ki-67 had low strokes (51.5%), PR + and PR- had high strokes (59.7% and 51%), her2- and her2 + had high strokes (51.2% and 72.2%).¹⁸

The discrepancy between the findings of the ER, PR, and HER2 results in RSUP Haji Adam Malik and the other studies was that the reliability of the standard anatomy pathology laboratory in Medan was widely suspected that it might affect the results of the immunohistochemistry test. The results of the IHC test have a major impact on the decision of the surgeon in managing breast cancer so that high precision values are required in the pathology anatomy laboratory.¹⁸

The drawback of this research was the limited number of samples relative to the number of patients with breast cancer in RSUP Haji Adam Malik Medan. Furthermore, the researchers did not investigate the hormonal status of the patient, such as menarche age, menopause age, first delivery age, overall parity and hormonal contraceptive usage. Hormonal status is important because breast cancer is a hormonal disorder and has been linked with PROM in many studies. Researchers have attempted to see the hormonal status of the research samples that met the inclusion criteria but did not obtain full data from the medical records. In addition, once the interview is held, the researcher must know the patient's cell phone number so that they can be notified. The number of the mobile phone was printed on the medical record, but not all of the numbers are still available.

V. CONCLUSION

Most of the breast cancer patients in RSUP Haji Adam Malik Medan from 2014-2016 were mostly aged 40-49 years, around 33 samples (34.7%) had high school education level and 95.8% did not have a family history of breast cancer.

Most of the breast cancer patients around 42 samples (44.2%) at stage IIIB, around 50 samples (52.6%) with T4b tumor, 40 samples (42.1%) metastasized on ipsilateral (N1) and 11 samples (40.7%) metastasized to the lung. Patients diagnosed with Invasive Ductal Carcinoma was 68 samples (71.6%). The majority samples was negative in estrogen receptors (ER) with a total of 70 samples (73.7%), 67 samples (70.5%) with negative in progesterone receptors, 31 samples (32.6%) with her2 positive, and 49 samples (51.6%) with a positive ki-67.

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