SUMEJ

Sumatera Medical Journal

PREVALENCE AND CHARACTERISTICS OF BREAST CANCER IN YOUNG WOMEN

Denny Rifsal Siregar1*, Andreas Christoper2

1 Department of Surgical Oncology, Haji Adam Malik General Hospital, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia
2 Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

Abstract. Breast cancer is a major health problem for women. This cancer is most often diagnosed and the leading cause of cancer deaths in women worldwide. Breast cancer in young women is associated with late diagnosis, aggressive biological characteristics, and poor prognosis. The objective of the study is to determine the prevalence and characteristics of young age breast cancer in Haji Adam Malik General Hospital Medan in 2013-2017. The study design was observational descriptive design with a cross-sectional approach. The study samples were medical records of young women diagnosed with breast cancer who were treated at Haji Adam Malik General Hospital Medan. The prevalence of breast cancer in young age women in Haji Adam Malik General Hospital Medan in 2013-2017 was 234 patients (15.2%). In this study, the samples that fulfilled the inclusion criteria were 153, with the majority characteristics of patients were 35-39 years old, stage III, histopathological type of invasive carcinoma of no special type, grade II, and clinical subtype of triple-negative. The prevalence of young age breast cancer is lower than old age breast cancer. Young women tend to be diagnosed with breast cancer in advanced stage and intermediate grade with aggressive biological characteristics.

Keyword : Young Age Breast Cancer; Stage; Histopathological Type; Grade; Clinical Subtype

1. Introduction

Cancer is a disease that can cause cells in the body to change and spread uncontrollably. When cancer cells are first discovered in the breast, it is called breast cancer. Most breast cancer cells will form a lump or mass called tumor. These malignant cells in breast cancer usually grow in breast tissue that appears in the lobules and ducts in the breast [1]. Risk factors for breast cancer can be distinguished into reproductive and non-reproductive factors. Reproductive factors are early menarche (<12 years), late menopause (>55 years), history of first pregnancy over the age of 30 years, never giving birth (nulliparity) and breastfeeding, and oral contraceptive use. Whereas non-reproductive factors are obesity, alcohol consumption, smoking, radiation history

---

*Corresponding author at: Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

E-mail address: denny.rifsal@usu.ac.id

during childhood, family history and genetic predisposition (BRCA1 or BRCA2 gene mutations)[2]-[3].

Breast cancer is the second most common cancer in the world and, so far, the most common cancer in women with an estimated incidence of 2.1 million diagnosed in 2018 (24.2% of all cancers). This disease is the most commonly diagnosed cancer in most countries (154 of 185 countries) and is also a leading cause of cancer death in more than 100 countries. Breast cancer is the fifth in the overall cause of cancer deaths (626,679 deaths) and while it is the highest cause of death from cancer in women. Indonesia is in the 8th rank for the highest number of breast cancer new cases and 5th rank for the highest number of cases of breast cancer deaths in the world in 2018[4].

Breast cancer can be diagnosed through triple assessment, namely clinical (history taking, physical examination), radiological and pathology examination. The assessment is a guide in diagnosis, determining the stage of breast cancer, determining the histopathological type, grading, and clinical subtypes of tumor that can be used in deciding therapy and the prognosis of breast cancer patients[5].

Breast cancer in young women is very rare. The cases with criteria for ages 20-39 years worldwide are approximately 243,096 new cases (11%) and 44,698 deaths from cancer[6]. They have major risk factors, such as heredity, mostly diagnosed with genetic mutations. Breast cancer in young women has unique characteristics, which are not found in older women, like aggressive biological characteristics (histopathological type and clinical subtype) and poor differentiation. In young women, breast cancer tends to be diagnosed in its advanced stage and higher grade breast tumors compared to older women[7]. This can lead to a worse prognosis than the prognosis of older premenopausal and postmenopausal women with breast cancer. Problems commonly found in young women are late diagnosis, lack of screening, and higher tumor growth rate[8].

Based on the description above, breast cancer is commonly found in the world, one of the countries is Indonesia, with high incidence and mortality. Breast cancer can be suffered by all ages, not only for older women but also for young women (<40 years) and has a poor prognosis. Therefore, this study was conducted to determine the prevalence and characteristics of breast cancer, such as stage, histopathological type, grade, and clinical subtype in young women (<40 years) at Haji Adam Malik General Hospital Medan in 2013-2017.

METHODS

The research design used in this study was observational descriptive with a cross-sectional design approach. The samples in this study were medical records of breast cancer patients younger than 40 years who were treated at Haji Adam Malik General Hospital Medan. The sampling technique in this study was consecutive sampling. In this study, the inclusion criteria are: 1) the first age of diagnosis of breast cancer are younger than 40 years; 2) the patient has undergone physical and pathology examination (histopathology and immunohistochemistry) and is fully recorded in the medical record; while the exclusion criteria are: 1) patients with cancer in other organs that are not breast cancer metastatis; 2) incomplete medical and diagnosis records. After collecting the samples, 153 medical records fulfilled the inclusion criteria of this study.

The variables studied included: 1) the age of the first diagnosis, with classifications of less than 25 years, 25-29 years, 30-34 years, and 35-39 years; 2) stage, with classifications of stage 0, stage I (A, B), stage II (A, B), stage III (A, B, C), and stage IV; 3) histopathological type, with classifications of invasive (NST, lobular, tubular) and in-situ breast cancer; 4) grade, with grade I, grade II, and grade III classifications; 5) clinical subtypes, with luminal A, luminal B, HER2-enriched, and triple-negative classifications.

Before the study was conducted, Ethical Clearance had been conducted and approved by the Ethics Committee of Faculty of Medicine USU. The data sources are secondary data, which is medical and diagnosis record data of the patients in 2013-2017 obtained at Medical Records Department and Department of Surgical Oncology at Haji Adam Malik General Hospital Medan. The processed data is analyzed using the Statistical Product and Service Solutions (SPSS) program.

RESULTS AND DISCUSSION

Among 1,543 breast cancer patients at Haji Adam Malik General Hospital Medan, 234 (15.2%) are younger than 40 years old. The population of young breast cancer patients in 2013, 2014, 2015, 2016, and 2017 were 33, 37, 58, 63, and 43, respectively. The amount of data that fulfilled the inclusion criteria, or samples in this study, were 153 data (Table 1).

Table 1 The prevalence of breast cancer in 2013-2017

Year	< 40 years		≥ 40 years		Breast cancer patients
	Frequency	Percentage (%)	Frequency	Percentage (%)	
2013	33	12,7	226	87,3	259
2014	37	15,2	244	84,8	281
2015	58	18,7	252	81,3	310
2016	63	18,2	284	81,8	347
2017	43	12,4	303	87,6	346
Total	**234**	**15,2**	**1.309**	**84,8**	**1.543**

Based on the patients' age at diagnosis, the median age was 35 (minimum and maximum age of 21 and 39). The majority age interval was 35-39 years (63.4%), followed by 30-34 years (26.1%), 25-29 years (9.2%), and <25 years (1.3%). Clinically, 1.3% and 14.4% of patients diagnosed with stage I and stage II (early-stage breast cancer), 49% with stage III (locally advanced), and 35.8% with stage IV (advanced stage). From breast tumors characteristics, the most common histopathological type was invasive carcinoma of no special type / ductal carcinoma (88.9%). The others were invasive lobular carcinoma (7.8%), invasive tubular carcinoma (2.6%) and inflammatory carcinoma (0.7%). No in-situ breast cancer data was found in this study. The patients with grade I, II, III, were 15.7%, 64%, and 20.3%, respectively. Triple-negative was the most clinical subtype found in young age breast cancer (31.4%), followed by luminal A (28.1%), luminal B (24.2%), and HER2-enriched (16.3%) (Table 2).

Table 2 The characteristics of young breast cancer (153 patients)

Characteristics	Frequency	Percentage (%)
Age at diagnosis (interval)		
< 25	2	1,3
25-29	14	9,2
30-34	40	26,1
35-39	97	63,4
Staging		
Stage I	2	1,3
Stage II	22	14,4
Stage III	75	49,0
Stage IV	54	35,3
Histopathological type		
Invasive carcinoma of no special type	136	88,9
Invasive lobular carcinoma	12	7,8
Invasive tubular carcinoma	4	2,6
Inflammatory carcinoma	1	0,7
Grading		
Grade I	24	15,7
Grade II	98	64,0
Grade III	31	20,3
Clinical subtype		
Luminal A	43	28,1
Luminal B	37	24,2
HER2-enriched	25	16,3
Triple-negative	48	31,4

Breast cancer in young women has a definition that varies between the ages of 35 or 40 years. To date, there is no consensus for defining breast cancer in 'young' and 'very young' women, with various studies using ages 30, 35, 40, and 45 years as the cutoff age in various research[7].

The prevalence of young age breast cancer in Haji Adam Malik General Hospital Medan in 2013-2017 is 234 patients, or 15.2% of all breast cancer cases, which the percentage is lower than old age breast cancer. Similar study has been carried out at Sanglah Hospital using medical record data in 2002-2012 and 2014-2016, with the proportions of breast cancer aged <40 years are 22.7% and 14% [9][10]. International Agency for Research on Cancer shows young age breast cancer cases in Asia are higher than those in America and Europe, according to breast cancer cases at <40 years of age which is Asia has the highest prevalence in the world[4]. Research conducted in America and Europe shows prevalence rate is 4%,[1,11] while the prevalence rate in Asia reached 26%[12][13].

The majority of breast cancers in young women in Haji Adam Malik General Hospital Medan occur in the age range of 35-39 years. This result is suitable with the study in Sanglah General Hospital with the majority of cases occured in the age range of 35-39 years. The increasing number of cases occurs along with increasing age. Other studies also state that breast cancer cases increase with increasing age in the age limit of <40 years[9][11][14].

Delay in diagnosis often occurs in young patients with breast cancer, which results in patients being first diagnosed with advanced and intermediate-high-grade breast cancer[9][13][15][16], caused by low awareness of patients for early detection (screening) and lack of patient knowledge about breast cancer. The delay can occur not only because patients just visit health facilities because of complaints about their breasts, but also because doctors who are less alert in diagnosing breast cancer and referring patients for immediate therapy. It is also difficult for doctors to diagnose young age breast cancer due to increased breast density of young women. In addition, more aggressive tumor biology and more rapid tumor progression in younger patients are indicative of more advanced disease at diagnosis[7][8][17][18].

Young women with breast cancer tend to have tumor with aggressive biological characteristics. Invasive carcinoma is mostly found in the tumor of the patients, with the majority type is invasive carcinoma of no special type / ductal carcinoma (NST). Most of the studies that have been carried out show that invasive carcinoma of a special type (NST) is the most histopathological type found in women, both young and old, with breast cancer[13][16][17].

Based on gene expression profiling analysis (IHC), most tumors of young age breast cancer have no hormone-receptor (ER, PR) and no HER2, or in the other words, the clinical subtype is triple-negative. Some studies also found triple-negative was the most clinical subtypes in women with breast cancer at the age of <40 years [19][20][21]. Immunohistochemical examination is a standard in determining breast cancer subtypes. Determination of subtypes in breast cancer will play a role in helping determine the type and prediction of systemic therapy response and prognosis of the patients[5]. The triple-negative subtype in young women has worse prognosis than that in older women, but the risk of recurrence and death do not increase in patients who have received therapy[22].

CONCLUSIONS AND FUTURE RESEARCH

The prevalence of breast cancer in young women (<40 years) is lower than the prevalence in older women who were admitted to Haji Adam Malik General Hospital Medan in 2013-2017. The majority characteristics of breast cancer in young women in this study were aged 35-39 years, who were diagnosed with aggressive and advanced biological characteristics, namely locally-advanced stage, histopathological type of invasive carcinoma of special type / NST, intermediate grade, and triple-negative clinical subtype.

Next researchers can look for a relationship between the characteristics found in breast cancer patients with young age (<40 years), and look for the relationship of hereditary (history of breast cancer in the family), reproductive (early menarche, history of contraceptive use) and non-reproductive (lifestyle) risk factors with the prevalence of breast cancer in young women.

REFERENCES

[1] American Cancer Society, "Breast Cancer Facts & Figures 2017-2018," *American Cancer Society, Inc*, 2017.

[2] M. Morrow, H.J. Burstein, J.R. Harris, "Malignant Tumors of the Breast," in *Cancer Principle & Practice of Oncology*, V.T. DeVita, T.S. Lawrence, S.A. Rosenberg, Eds. Philadelphia: Lippincott Williams & Wilkins, 2015, 1117-1152.

[3] M. Piccart, T. Gathani, D. Zardavas, H.A. Azim Jr, C. Sotiriou, G. Viale, et al, "Cancer of the Breast," in *Oxford Textbook of Oncology*, D.J. Kerr, D.G. Haller, C.J. van de Velde, M. Baumann, Eds. United Kingdom: Oxford University Press, 2016, 546-559.

[4] F. Bray, J. Ferlay, I. Soerjomataram, R.L. Siegel, L.A. Torre, A. Jemal, "Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries," *CA: A Cancer Journal for Clinicians*, vol. 68, no. 6, pp. 394-424. 2018.

[5] H. Purwanto, D. Handojo, S.J. Haryono, W.A. Harahap, Eds, *Panduan Penatalaksanaan Kanker Payudara*. Jakarta: PERABOI, 2015.

[6] J. Ferlay, M. Ervik, F. Lam, M. Colombet, L. Mery, M. Piñeros, et al, "Global Cancer Observatory: Cancer Today," *International Agency for Research on Cancer*, 2018 Sep. [Online] Available: https://gco.iarc.fr/today.

[7] H.B. Lee, W. Han, "Unique Features of Young Age Breast Cancer and Its Management," *Journal of Breast Cancer*, vol. 17, no.4, pp. 301-307. 2014.

[8] D.S. Eugênio, J.A. Souza, R. Chojniak, A.G. Bitencourt, L. Graziano, E.F. Souza, "Breast cancer features in women under the age of 40 years," *Revista da Associacao Medica Brasileira*, vol. 62, no. 8, pp. 755-761. 2016.

[9] M.D. Hartaningsih, W. Sudarsa, "Kanker Payudara pada Usia Muda di Bagian Bedah Onkologi Rumah Sakit Umum Pusat Sanglah Denpasar Tahun 2002-2012," *EUM*, vol. 3, no.6. 2014.

[10] P.D. Partini, I.W. Niryana, P.A. Adiputra, "Karakteristik Kanker Payudara Usia Muda di Subbagian Bedah Onkologi Rumah Sakit Umum Pusat Sanglah Tahun 2014-2016," *ISM*, vol. 9, no. 1, pp. 76-79. 2018.

[11] Cancer Research UK. "Breast cancer incidence (invasive) statistics," *Cancer Research UK*, 2018. [Online] Available: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/incidence-invasive

[12] I. Mehdi, E.A. Monem, B.J. Bahrani, S.A. Kharusi, A.M. Nada, J.A. Lawati, et al, "Age at diagnosis of female breast cancer in Oman: Issues and implications," *South Asian Journal of Cancer*, vol.3, no.2, pp. 101-106. 2014.

[13] S.K. Lee, S.W. Kim, J.H. Yu, J.E. Lee, J.Y. Kim, J. Woo, et al, "Is the high proportion of young age at breast cancer onset a unique feature of Asian breast cancer?," *Breast Cancer Research and Treatment*, vol.173, no.1, pp.189-199. 2019.

[14] T.H. Keegan, D.J. Press, L. Tao, M.C. DeRouen, A.W. Kurian, C.A. Clarke, et al, "Impact of breast cancer subtypes on 3-year survival among adolescent and young adult women," *Breast Cancer Research*, vol. 15, no. 5, pp. R95. 2013.

[15] C. Villarreal-Garza, A. Mohar, J.E. Bargallo-Rocha, F. Lasa-Gonsebatt, N. Reynoso-Noverón, J. Matus-Santos, et al, "Molecular Subtypes and Prognosis in Young Mexican Women With Breast Cancer," *Clinical Breast Cancer*, vol.17, no.3, pp. e95-e102. 2017.

[16] M.C. Cormedi, E.F. Lopes, S. Maistro, R.A. Roela, M.A. Folgueira, "Clinical stage and histological type of the most common carcinomas diagnosed in young adults in a reference cancer hospital," *Clinics (São Paulo)*, vol.73, suppl 1, pp. e656s. 2018.

[17] J. Bakkach, M. Mansouri, T. Derkaoui, A. Loudiyi, M. Fihri, S. Hassani, et al, "Clinicopathologic and prognostic features of breast cancer in young women: a series from North of Morocco," *BMC Women's Health*, vol.17, no.1, pp.106. 2017.

[18] G.A. Dyanti, N.L. Suariyani, "Faktor-Faktor Keterlambatan Penderita Kanker Payudara dalam Melakukan Pemeriksaan Awal ke Pelayanan Kesehatan," *Kemas*, vol.11, no.2, pp. 96-104. 2016.

[19] E.O. Jenkins, A.M. Deal, C.K. Anders, A. Prat, C.M. Perou, L.A. Carey, et al, "Age-Spesific Changes in Intrinsic Breast Cancer Subtypes: A Focus on Older Women," *The Oncologist*, vol. 19, no. 10, pp. 1076-1083. 2014.

[20] M. Kolečková, Z. Kolář, J. Ehrmann, G. Kořínková, R. Trojanec, "Age-associated prognostic and predictive biomarkers in patients with breast cancer," *Oncology Letters*, vol. 13, no. 6, pp. 4201-4207. 2017.

[21] G. Curigliano, H.J. Burstein, E.P. Winer, M. Gnant, P. Dubsky, S. Loibl, et al, "De-escalating and escalating treatments for early-stage breast cancer: the St. Gallen International Expert Consensus Conference on the Primary Therapy of Early Breast Cancer 2017," *Annals of Oncology*, vol. 28, no. 8, pp. 1700-1712. 2017.

[22] H. Alabdulkareem, T. Pinchinat, S. Khan, A. Landers, P. Christos, R. Simmons, et al, "The impact of molecular subtype on breast cancer recurrence in young women treated with contemporary adjuvant therapy," *The Breast Journal*, vol. 24, no. 2, pp. 148-153. 2018.