Original Research Article

STUDY OF EPIDEMIOLOGICAL PATTERNS AND CLINICAL PROFILES OF BREAST CANCER IN YOUNG PATIENT: A RETROSPECTIVE STUDY AT DR. MOEWARDI SURAKARTA

ABSTRACT

Introduction: Breast cancer remains a major health problem and a top priority for biomedical research. The incidence of this aggressive disease is around 1,700,000 new cases each year; This figure shows the low level of efforts to prevent this disease. About 12% of breast cancer cases occur in women aged ≥45 years. Unlike breast cancer in older women and the incidence of metastatic breast cancer has significantly increased in younger women over the past 30 years.
Aims: This study aims to identify the characteristics of risk factors on young women with breast cancer patients.
Study design: This study was a retrospective descriptive study, with 182 subjects of young women breast cancer patient at the Department of Oncology, RSUD Dr. Moewardi Surakarta in 2021 - 2023.
Place and Duration of Study: Sample: Department of Oncology, RSUD Dr. Moewardi Surakarta in 2021 - 2023.
Methodology: This study was a retrospective descriptive study, with 182 subjects of young women breast cancer patient at the Department of Oncology, RSUD Dr. Moewardi Surakarta in 2021 - 2023. The study will be conducted using medical record of the hospital.
Results: There were some risk factors that we found. There were young age at diagnosis, nulliparity, family history of malignancies, breastfeeding, hormonal contraception, children count, and age at first pregnancy.
Conclusion: This study concludes some risk factors of breast cancer in young women.

Keywords: breast cancer, young women, risk factors, demography

1. INTRODUCTION

Breast cancer is the most frequently diagnosed malignancy in women. Most cases of breast cancer arise due to abnormal cell growth in the mammary gland ducts (50-70%) or mammary gland lobules (10-15%). This is what makes this tumor called adenocarcinoma. A small percentage of breast tumors are sarcomas, these tumors originate from stromal cells or muscle cells. Other types and subtypes of breast cancer are less common.[1]

Breast cancer is an invasive cancer that often occurs in women throughout the world. According to GLOBOCAN, in 2020 female breast cancer surpassed lung cancer as the most frequently diagnosed cancer with an estimated 2.3 million new

cases (11.7%). Breast cancer mortality rates are much higher in developing countries than in developed countries (15.0 vs. 12.8 /100,000). In women, breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death followed by colorectal cancer (incidence) and lung (mortality rate)[2]

Most of the breasts consist of glandular tissue (which produces milk) and fat. However, the ratio of glandular tissue to fat varies between individuals. Breasts are greatly influenced by the sex hormone estrogen. As menopause approaches, estrogen levels decrease which also reduces the amount of glandular tissue. The pectoralis major muscle forms the base of the breast extending from the second to sixth ribs in early human life, but can extend below the sixth rib as the breast matures and hangs down. The breasts are attached to the pectoralis major fascia by Cooper's ligaments but these ligaments are flexible and allow movement in the breasts in most women. Cooper's ligaments become stretched over time and age eventually resulting in ptotic breasts due to the gravity of the lower breast being fuller than the upper. On the lateral edge of the breast Spence's tail extends to the axilla. The nipple is usually located just above the inframammary crease and is consistently found parallel along the mid-clavicular line and fourth rib.[3]

Breast cancer is one of the most frequently diagnosed cancers in adolescent and young adult women aged <40 years. Currently, breast cancer in adolescent and young adult women accounts for approximately 7% of all breast cancer diagnoses in all age groups. Younger age at menarche and older age at menopause increase the risk of breast cancer. The risk of breast cancer is approximately 20% higher among girls who start menstruating before age 11 compared with those who start menstruating at age 13.
Childbearing at a relatively older age, smaller family size, short duration of breastfeeding, and use of hormonal contraception have been associated with an increased risk of breast cancer. In contrast, women who had their first child at a younger age and had more children were associated with a reduced risk of breast cancer.[4]
Global gene expression profiling studies classify breast cancer into 5 intrinsic subtitles with hierarchical clustering; namely luminal a, luminal b, overexpression of HER 2, breast cancer such as basal cells (BLBC), and tumors that resemble normal conditions. Many factors can determine the prognosis, one of which is the morphological description of tumor cells, namely the histology type of the tumor. The medullary and mucinous types show a better prognosis than the ductal type. 85% of the ductal type have a poor prognosis. Nuclear grading is determined from points 1 2 and 3, namely tubular appearance, nuclear pleomorphism, and nuclear to cystoplasm ratio. Signs of infiltration of the lymphoid vessels also determine a poor prognosis. [5,6]

Young women with breast cancer tend to have more aggressive disease than older women and have a lower survival rate. These include higher estrogen receptors, higher histopathological grade, and more negative subtypes (38%) compared to older age (26%). Low outcomes are found in young breast cancer due to the high clinical stage at diagnosis, with larger tumor size, and more positive axillary lymph nodes. From several studies, it has been concluded that young breast cancer has a higher recurrence rate with shorter Disease Free Survival (DFS) and Overall Survival (OS) than older breast cancer.[7]

The purpose of this study is to investigate the unique characteristics and potential risk factors affecting young women diagnosed with breast cancer. By delving into this demographic subset, the research aims to uncover specific factors that may contribute to the development or progression of breast cancer in young women. Through comprehensive analysis, including factors such as genetic predisposition, lifestyle choices, environmental influences, and hormonal factors, the study seeks to provide valuable insights into understanding the distinct profile of breast cancer among young women. Ultimately, the findings aim to inform more targeted preventive measures, early detection strategies, and personalized treatment approaches tailored to the needs of this vulnerable population.

2. MATERIAL AND METHODS

This research is a descriptive study with a retrospective approach to describe the profile of breast cancer in young women at RSUD Dr. Moewardi Surakarta. Employing a purposive sampling technique, subjects fulfilling the predetermined inclusion criteria will be selected within a specified timeframe to ensure an adequate sample size. The study will encompass all young women diagnosed with breast cancer at Dr. Moewardi Regional Hospital between 2021 and 2023, ensuring that patients have received informed consent before their inclusion in the study. Relevant data about risk factors will be extracted from patients' medical records for analysis.

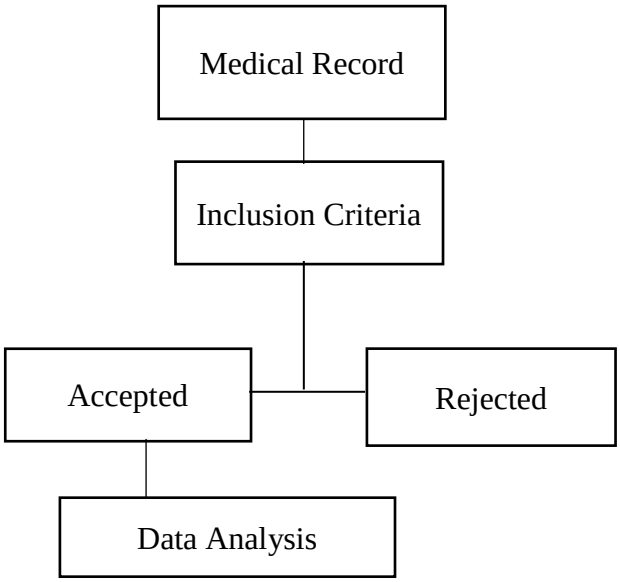

Fig 1. The adopted Methodological Framework

Inclusion Criteria
Young women: aged ≤40 years
Complete patient data
Histopathology results can be tracked

Exclusion Criteria
Incomplete data.

3. RESULTS AND DISCUSSION

This study involved young female patients (aged ≤40 years) who were diagnosed with breast cancer and were treated at the Department of Surgical Oncology, RSUD Dr. Moewardi Surakarta. The total research sample was 182 patients. The research was carried out using a retrospective method, by exploring risk factor data from medical records at RSUD Dr. Moewardi. This research has been approved by the Health Research Ethics Committee of Dr. Moewardi General Hospital as stated in the letter number 847/VI/HREC/2022.

Table 1. Patient Characteristics

Characteristics	Frequency) and percentage (%) Mean ± SD
Patient Age	(n = 182) 36.18 ± 3.918
<30 years	16 (8.8%)
≥30 years	166 (91.2%)
Age at Diagnosis	33.23± 3.73
30 – 40 years old (young)	148 (81.3%)
<30 years (very young)	34 (18.7%)
Married Age	22.29 ± 6.126
Not married yet	9 (4.9%)
≤20 years	42 (23.1%)
21-30 years old	130 (71.4%)
>30 years	1 (0.5%)
Age at First Pregnancy	24.35 ± 4.142
Never been pregnant	17 (9.3%)
≤20 years	29 (15.9%)
21-30 years old	125 (68.7%)
>30 years	11 (6%)
Family History with Ca Mammae	
There isn't any	138 (75.8%)
There is	44 (24.2%)
Breast-feed	
Yes	143 (78.6%)
No	39 (21.4%)
Contraception	
No contraception	37 (20.3%)
Nonhormonal	15 (8.2%)
Hormonal	130 (71.4%)
Duration of Contraception	
< 10 years	138 (75.8%)
≥ 10 years	7 (3.8%)
No contraception	37 (20.3%)
Number of children	
Have no children	23 (12.6%)
1-2 children	124 (68.1%)
≥3 children	35 (19.2%)
Disease Stage	
EBC	43 (23.6%)
LABC	80 (44%)
MBC	59 (32.4%)

Source: Primary data

From the data collection carried out, we obtained the depiction of young woman who was diagnosed with breast cancer at RSUD Dr. Moewardi during the period 2021 - 2023 there were 182 patients. Of the total 182 patients, 34 (18.7%) were categorized as very young (<30 years) at diagnosis. The average patient age in general was 36.18 ± 3.918 with the average patient age at diagnosis being 33.23 ± 3.73. The youngest age at diagnosis was 25 years, and the oldest age was 39 years.

A total of 75 (41.2%) patients were diagnosed when they were <40 years old. A total of 9 (4.9%) patients were never married, and 17 (9.3%) patients had never been pregnant. A total of 44 (24.2%) patients had a family history of breast cancer. Of a total of 182 patients, it was found that 39 (21.4%) patients had never breastfed. A total of 37 (20.3%) patients had never used contraception, and 130 (71.4%) patients used hormonal contraception. The duration of hormonal contraceptive use was more commonly found to be less than 10 years, namely in 138 (75.8%) patients. Patients who did not have children were 23 (12.6%).

Data on the distribution of disease stages illustrates the predominance of the Locally Advanced Breast Cancer (LABC) stage at 80 (44%), followed by the Metastatic Breast Cancer (MBC) category at 59 (32.4%) and the Early Breast Cancer (EBC) stage at 43 (23.6%).

To determine the characteristics of the stage of the disease, a cross-tabulation examination was carried out between the characteristics of age at diagnosis, marriage, pregnancy, breastfeeding history, contraceptive history, family history, and number of children. From this examination, it was found that 40 (22%) patients were in the EBC stage, with the highest number being in the LABC stage, 65 (35.7%) in the age range of 30-40 years. In the more severe stage, there were 43 (23.6%) patients aged 30-40 years.

Table 2. Tumor Characteristics

Tumor Characteristics	Metastasis		
	Not metastatic	Local and Regional Infiltration Distant	Metastasis
Histology			
ductal	21 (11.5%)	61 (33.5%)	56 (30.8%)
lobular	16 (8.8%)	14 (7.7%)	4 (2.2%)
other	5 (2.7%)	4 (2.2%)	1 (0.5%)
Luminal			
Luminal B	19 (10.4%)	42 (23.1%)	19 (10.4%)
Luminal A	19 (10.4%)	8 (4.4%)	5 (2.7%)
TNBC	0	8 (4.4%)	19 (10.4%)
HER2	4 (2.2%)	21 (11.5%)	18 (9.9%)

Source: Primary data

In general, the age range 21-30 has the highest percentage of all stages of the disease. The highest number of married-age figures with the MBC stage was found at 34 (18.7%) and at the LABC stage, it was 58 (32.4%). Meanwhile, the rate at first pregnancy experienced a similar thing, with the highest rate at the LABC stage at 58 (31.9%) and at the MBC stage at 34 (18.7%). In the interim conclusion, the early age of marriage and first pregnancy are at risk of experiencing a higher stage.

Table 3. Tumor Stages based on Patient Characteristics

Tumor Characteristics	Stage		
	EBC	LABC	EBC
Age at Diagnosis			
30 – 40 years old (young)	40 (22%)	65 (35.7%)	43 (23.6)
<30 years (very young)	3 (1.6%)	15 (8.2%)	16 (8.8%)
Married Age			
Not married yet	1 (0.5%)	2 (1.1%)	6 (3.3%)
≤20 years	10 (5.5%)	19 (10.4%)	13 (7.1%)
21-30 years old	32 (17.6%)	58 (32.4%)	40 (21.4%)
>30 years	0	1 (0.5%)	0
Age at First Pregnancy			
Never been pregnant	2 (1.1%)	4 (2.2%)	11 (6%)
≤20 years	6 (3.3%)	13 (7.1%)	10 (5.5%)
21-30 years old	33 (18.1%)	58 (31.9%)	34 (18.7%)
>30 years	2 (1.1%)	5 (2.7%)	4 (2.2%)
Family History with Ca Mammae			
There isn't any	40 (22%)	64 (35.2%)	34 (18.7%)
There is	3 (1.6%)	16 (8.8%)	25 (24.2%)
Breast-feed			
Yes	38 (20.9%)	68 (37.4%)	37 (20.3%)
No	5 (2.7%)	12 (6.6%)	22 (12.1%)
Contraception			
No contraception	4 (2.2%)	14 (7.7%)	19 (10.4%)
Nonhormonal	5 (2.7%)	7 (3.8%)	3 (1.6%)
Hormonal	34 (18.7%)	59 (32.4%)	37 (20.3%)
Duration of Contraception			
< 10 years	36 (19.8%)	63 (34.6%)	39 (21.9%)
≥ 10 years	3 (1.6%)	3 (1.6%)	1 (0.5%)
No contraception	4 (2.2%)	14 (7.7%)	19 (10.4%)
Number of children			
Have no children	2 (1.1%)	6 (3.3%)	15 (8.2%)
1-2 children	26 (14.3%)	60 (33%)	38 (20.9%)
≥3 children	15 (8.2%)	14 (7.7%)	35 (19.2%)

Sumber : Data primer

There were 25 (24.2%) family histories of mammary Ca in the MBC stage, followed by 16 (8.8%) in the LABC stage. In general, the incidence rate in patients who do not have a family history of Ca mammae is still higher. A history of breastfeeding is reported to have a higher percentage of the incidence of LABC and MBC stages. At the MBC stage, 37 (20.3%) and LABC were found in 68 (37.4%) patients who had a previous history of breastfeeding. Patients with a history

of using hormonal contraception had a higher risk of disease stage, with 59 (32.4%) LABC stage and 37 (20.3%) MBC stage. Meanwhile, patients with several children in the range 1-2 had a higher stage risk, where LABC was found in 60 (33%) and MBC in 38 (20.9%).

Table 4. Tumor Characteristics

Tumor Characteristics	Stage		
	EBC	LABC	MBC
Histology			
ductal	22 (12.1 %)	61 (33.5%)	55 (30.2%)
lobular	16 (8.8%)	15 (8.2%)	3 (1.6%)
other	5 (2.7%)	4 (2.2%)	1 (0.5%)
Luminal			
Luminal B	19 (10.4 %)	41 (22.5%)	20 (11%)
Luminal A	19 (10.4 %)	9 (4.9%)	4 (2.2%)
TNBC	0	8 (4.4%)	19 (10.4%)
HER2	5 (2.7%)	22 (12.1%)	6 (8.8%)

Sumber : Data primer

In this study, the results were obtained in the form of images of young women with breast cancer at RSUD Dr. Moewardi. Of a total of 182 patients, 34 (18.7%) were categorized as very young (<30 years) at diagnosis. The average patient age in general was 36.18 ± 3.918 with the average patient age at diagnosis being 33.23 ± 3.73. The youngest age at diagnosis was 25 years, and the oldest age was 39 years. This supports various previous studies related to the incidence of breast cancer in young women. Research by Fernandes et al, stated that the average age of occurrence of breast cancer in young women was 36.1 years.[8] The majority of younger women (88%) had asymptomatic cancer, whereas the majority of older women (63.1%) were more likely to have cancer detected by mammography ($P < 0.001$).

A total of 17 (9.3%) patients in this study had never been pregnant. The age of first pregnancy ranges from 21-30 years. Even so, there are still patients who experience pregnancy before the age of 20 years. This is related to the risk of breast cancer due to nullipara. This is by previous studies by Winters et al. In this study, it was stated that nulliparity is a risk factor for breast cancer, and this risk is most obvious when compared with the risk in women who give birth at a relatively young age. Nulliparous women have a 20%–40% higher risk of developing postmenopausal breast cancer compared to women who first gave birth before the age of 25 years. The risk of breast cancer increases with age at first birth and is lower in women who gave birth to their first child when they were young than in nulliparous women.[9]

In this study, 44 (24.2%) patients had a family history of breast cancer. In previous studies, it was stated that a family history of breast cancer influences the incidence of breast cancer in young women. However, this association did not have a significant effect ($p>0.05$) in breast cancer cases in young women compared to women >40 years old. In this study, there were 80 cases of LABC stage (locally advanced breast cancer) and 59 cases of MBC stage (metastatic breast cancer). This figure shows a tendency for disease aggressiveness in young women's breast cancer cases. In previous studies, it was stated that breast cancer is a heterogeneous disease consisting of certain biological and molecular subtypes.[8,10]

Of a total of 182 patients, it was found that 39 (21.4%) patients had never breastfed. Among the many risk factors for developing breast cancer, breastfeeding is one known protective factor. Pregnancy and breastfeeding cause many

physiological changes in the breasts. These unique physiological changes occur due to hormonal changes that result in an increase in breast volume accompanied by nodularity, firmness, and increased parenchymal density. This change in density is one of the protective factors for breast cancer in young women.[9]

A total of 37 (20.3%) patients had never used contraception, and 130 (71.4%) patients used hormonal contraception. The duration of hormonal contraceptive use was more commonly found to be less than 10 years, namely in 138 (75.8%) patients. Patients who did not have children were 23 (12.6%). Considering that the development of breast cancer is caused by a combination of several biological, psychological, and environmental factors, including exogenous hormone intake, the causal mechanism cannot be linked directly to one risk factor alone. In addition, female hormones play an important role during the development of sexual characteristics in the mammary glands, acting as mitogens capable of promoting the development of various types of cancer through various receptor-dependent signaling pathways.[11,12]

Several things need to be considered regarding the limitations of this research. The method of retrospective can limit the information needed. Different risk factors may need to be explored more to help achieving a preventive solution for breast cancer in young women.

4. CONCLUSION

This study on breast cancer in young women reveals significant findings: a notable proportion of cases occur in those under 30, often with asymptomatic cancer. While nulliparity and family history were identified as risk factors, they didn't significantly influence incidence compared to older women. The aggressive nature of the disease in young women, shown by high rates of advanced stages, emphasizes the need for early intervention.

Breastfeeding emerged as a protective factor, while the impact of hormonal contraception warrants further investigation. However, the study acknowledges limitations, like its retrospective nature, suggesting the need for more research to inform better preventive strategies.

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