

CHARACTERISTICS OF IMMUNOHISTOCHEMISTRY EXAMINATION OF BREAST CANCER IN MANGUSADA HOSPITAL PERIOD 2022-2024

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ABSTRACT

Background: Breast cancer ranks first in the number of cancer cases as well as being the largest cause of cancer deaths in the world each year. In Indonesia, breast cancer is an urgent public health issue, yet it is clear that the burden of breast disease in Indonesia is considerable, influenced by several factors such as socioeconomic disparities, cultural beliefs, and limited access to healthcare, especially in Bali which is a popular tourist destination, which faces unique challenges in terms of breast health due to the large number of visitors and the potential for delayed diagnosis or inadequate follow-up. Immunohistochemical profiling examination has been widely used as a basis in classifying breast cancer molecularly. Therefore, a comprehensive analysis of the geographical distribution of breast cancer cases as well as immunohistochemical profiling is essential for further prevention and treatment, especially in Bali.

Methods: This retrospective study aimed to analyze the distribution of breast cancer from 2022 to 2024. Data was extracted from the hospital's medical record based on age, breast cancer diagnosis as well as immunohistochemistry results during the specified period. Statistical analysis was performed using SPSS 26.0 software.

Results: This study identified 182 samples, of which the most common age range was >50 years, 111 cases (60.98%) with the most common diagnosis being Invasive Carcinoma of no special type, 149 cases (81.86%). Most of the cases were grade II, namely 108 (59.34%). Based on subtypes, luminal B and HER-2 positive/ HER-2 Enriched were the dominant subtypes with 82 cases (45.05%) and 38 cases (20.87%) respectively, followed by triple negative/basal-like with 32 cases (17.58%) and luminal A with 28 cases (15.38%).

Conclusion: This study showed a wide variety of samples based on age, diagnosis, grade and immunohistochemical profile of breast cancer patients. Age showed a significant association between age and breast cancer prevalence and a variety of histologic types of breast cancer, with Invasive carcinoma of no special type being the most common subtype and grade II is the most common. By subtype, luminal B was the predominant case.

Keywords: breast cancer, immunohistochemical examination, Bali

INTRODUCTION

Breast cancer ranks first in the number of cancer cases as well as being the biggest cause of death from cancer in the world every year. According to WHO (2020) the prevalence of breast cancer is 2,261,419 cases where this cancer is mostly suffered by women. There is an 88% higher incidence rate in developing countries than in developed countries (55.9 and 29.7 per 100,000, respectively) and has a mortality rate of 17%. The incidence of the disease is expected to increase worldwide. Meanwhile, according to GLOBOCAN data in 2020, it is known that breast cancer is a cancer disease with the highest percentage of new cases, which is 11%, and the percentage of deaths due to breast cancer is 6.9%.¹⁻³

In Indonesia breast cancer is the second highest incidence cancer after cervical cancer and there is a tendency to increase from year to year. Most breast malignancies come at an advanced stage. The number of

breast cancer in Indonesia is found to be approximately 65,858 new cases every year (273,523,621 population).¹⁻³

The rapid advancement of science and technology in the field of medicine has offered various therapeutic options that can be used for breast cancer patients. These include surgery, chemotherapy, radiotherapy, hormonal therapy and targeting therapy. Immunohistochemical profile examination has been widely used as a basis for selecting hormonal therapy and targeting therapy. Immunohistochemical examination can detect the types of cancer cell hormone receptors, namely estrogen receptor (ER) and progesterone receptor (PR), as well as the expression of human epidermal growth factor receptor-2 (HER2).^{4,6,7} These hormone receptors can be found in both normal and cancer cells and have a role in cell growth when they bind to hormones. Meanwhile, HER-2 belongs to the epidermal growth factor receptor (EGFR) class whose expression is related to the growth and differentiation process of various normal epithelial cells. In breast cancer cells with HER-2

overexpression, there is an increase in cell growth and differentiation activity. HER-2 is positive in about 18-20% of breast cancers.⁸ The expression of ER, PR, and HER-2 on immunohistochemical examination is the basis for molecular classification of breast cancer.

Based on this classification, breast cancer is divided into several subtypes namely luminal A, luminal B, HER-2 enriched and basal-like/triple negative. Each type has different characteristics both in terms of the therapy given and the prognosis. Hormonal therapy is given to patients with positive hormone receptor examination such as the luminal type. While targeting therapy is given to patients who show positive HER-2 results. As a reference for prognosis, some literature says that the prognosis tends to be good if there is ER and or PR expression on immunohistochemical examination. Conversely, the prognosis is poor if there is a positive HER-2 result and a negative hormonal receptor.^{4,5,8}

Based on the description above, immunohistochemical examination is very important in breast cancer patients both as a determination of therapy and patient prognosis. The purpose of this research is to knowing the description of immunohistochemical profiles in breast cancer patients at RSUD. Mangusada Bali for the period 2022-2024.

METHODS

This study employs a cross-sectional design. A total of 182 samples was taken using a total sampling system. This study is a retrospective descriptive study, by looking back at patient data diagnosed with breast cancer, so that data on immunohistochemical examination in the period 2022-2024 are obtained. Data is secondary data obtained from medical records of breast cancer patients at the Anatomical Pathology Laboratory of RSUD. Mangusada for the period 2022-2024. Inclusion criteria included all data on breast cancer patients who had performed immunohistochemical examinations and were accompanied by information in the form of patient age, pathology diagnosis, grade and immunohistochemical

examination. The exclusion criteria were the data collected and then processed using the SPSS 26.0 program.

RESULTS

This study aimed to investigate the prevalence and distribution of breast cancer in a specific population over a three-year period (2022-2024) at Mangusada Hospital. A total of 182 cases were identified during this time, providing valuable insight into the characteristics of breast cancer in the study area. The number of cases and characteristics by age are presented in **(Table 1)**. The table shows that a total of 182 cases were identified during the period, with the highest number of cases found in 2024 at 101 (55.49%). The distribution of cases by age is that most cases are in the age group > 50 years, namely 111 (60.98%). A total of 182 breast cancer cases were analyzed, showing a variety of histological subtypes **(Table 2)**. The most common diagnosis was Invasive Carcinoma of no special type, with 149 cases (81.86%). Followed by Invasive Lobular Carcinoma with 15 cases (8.24%). The Mix Invasive Carcinoma with Invasive Lobular Carcinoma type was 9 cases (4.94%).

A total of 182 breast cancer cases were analyzed over a three-year period (2022-2024), showing a variety of grades based on histopathological diagnosis **(Table 3)**. The most common histopathologic grade was grade II, with 108 cases (59.34%). This was followed by grade III with 71 cases (39.01%) and grade I with 3 cases (1.64%).

Based on immunohistochemical profiles, 182 patients analyzed showed a variety of immunohistochemical profile subtypes **(Table 4)**. The most common immunohistochemical profile (subtype) was Luminal B subtype with 82 cases (45.05%), the second most common was Her-2 Enriched subtype with 38 cases (20.87%), followed by Tripple negative/basal-like with 32 cases (17.58%) and Luminal A with 28 cases (15.38%)

Table 1. Distribution of Breast Cancer Cases by Age

| | Year | | | Total (n = 182 (100%)) |
|--------------|-------------|-------------|--------------|------------------------------|
| | 2022 | 2023 | 2024 | |
| Cases | 30 (16,48%) | 51 (28,02%) | 101 (55,49%) | 182 (100%) |
| Age | | | | |
| 30-40 | 0 (0%) | 6 (3,29%) | 9 (4,94%) | 15 (8,24%) |
| 41-50 | 12 (6,59%) | 16 (8,79%) | 28 (15,38%) | 56 (30,76%) |
| > 50 | 18 (9,89%) | 29 (15,93%) | 64 (35,16%) | 111 (60,98%) |

Table 2. Distribution of Breast Cancer cases based on histopathology diagnosis for the period 2022-2024

| Histologic type | Cases |
|---|--------------|
| Invasive Carcinoma of no special type | 149 (81.86%) |
| Invasive Lobular Carcinoma | 15 (8,24%) |
| Mix Invasive Carcinoma with Invasive Lobular Carcinoma | 9 (4,94%) |
| Invasive Carcinoma of no special type with neuroendocrine feature | 5 (2,74%) |
| Mucinous Carcinoma | 2 (1,09%) |
| Solid Papillary Carcinoma | 1 (0,54%) |
| Metaplastic Carcinoma | 1 (0,54%) |

Table 3. Distribution of Breast Cancer cases based on histopathology grade

| | Year | | | Total (n = 182 (100%)) |
|---------|-------------|-------------|-------------|-----------------------------------|
| | 2022 | 2023 | 2024 | |
| Grade I | 1 (0,54%) | 0 (0%) | 2 (1,09%) | 3 (1,64%) |
| II | 19 (10,43%) | 33 (18,13%) | 56 (30,76%) | 108 (59,34%) |
| III | 10 (5,49%) | 18 (9,89%) | 43 (23,62) | 71 (39,01%) |

Table 4. Subtype distribution of breast cancer immunohistochemical profiles for the period 2022-2024

| Immunohistochemical Profile (Subtype) | Cases |
|--|--------------|
| Luminal A | 28 (15,38%) |
| Luminal B | 82 (45,05%) |
| Her-2 <i>Enriched</i> | 38 (20,87%) |
| <i>Tripple negative/ basal-like</i> | 32 (17,58%) |

DISCUSSION

This study examined the prevalence of breast cancer in a specific population. Our findings showed a significant predominance of breast cancer at 182 cases. This alarming number is in line with global findings where the global burden increased 10-fold geographically in 2018. Although the prevalence rates observed in our study align with global trends, it is important to contextualize these findings within the specific demographic and socioeconomic factors of the target population.^{9,10}

This study showed a significant association between age and the likelihood of developing breast cancer. In particular, we observed a marked increase in the incidence of breast cancer with age, especially among women aged >50 years. The observed age distribution of breast cancer cases is in line with established epidemiologic data, where the highest-risk group is the 8-9% of women diagnosed with IBC before the age of 75 years.^{9,10} This pattern is consistent with the notion that age-related hormonal changes, genetic factors, and

cumulative exposure to risk factors contribute to the development of breast cancer.¹¹

This study showed a predominance of Invasive Carcinoma of no special type accounting for 81.86% of all cases (Table 2). The observed distribution of histologic types is in line with the global trend, where the majority of all breast cancer cases are of no special type (NST).^{9,12} Several factors may underlie the histomorphologic and age-related differences in breast cancer prevalence, including hormonal factors, where menopause is strongly associated with an increased risk of breast cancer. Other factors include genetic factors, where BRCA1 and BRCA2 mutations may increase breast cancer risk, and the effect may become more pronounced with age. Lastly, lifestyle factors, such as cumulative exposure to risk factors like obesity, smoking and lifelong alcohol consumption may contribute to the development of breast neoplasms in older age groups. In addition, environmental factors, exposure to environmental toxins, radiation and lifestyle may play a role in determining

breast neoplasms and their subtypes. Identification of histologic type is critical to guide treatment decisions and predict prognosis. This study highlights the importance of accurate histologic diagnosis and the need for ongoing research to develop targeted therapies for specific breast cancer subtypes.¹³

Our study showed a predominance of grade II with 59.34% of all cases (Table 4). Low grade histopathologic grades are often found in western regions, while in Indonesia, grade II and III tend to be the most frequent histopathologic grading.¹³

Based on the molecular classification of breast cancer, the incidence of breast cancer at RSUD. Mangusada Bali is dominated by luminal B subtype with a percentage of 45.05%, followed by HER-2 positive/HER-2 enriched subtype with a percentage of 20.87%, triple negative/basal-like with a percentage of 17.58%, then luminal A at 9.5%. Research results on these breast cancer subtypes vary. Research in Morocco by Fatemi et al with 390 samples showed a difference where the luminal B subtype was dominant with a presentation of 41.8% followed by luminal A at 30.5%.¹⁵ However, a study by Munjal et al in India with 107 samples showed that the luminal A subtype was the most common with a percentage of 37.4%, followed by the HER-2 positive subtype at 29%.¹⁴ Very few studies have shown results with high incidence rates in the basal-like/triple negative subtype.

This difference may occur due to various factors. Luminal subtype B is the most common, it has a higher proliferation of cancer cells and has a worse prognosis than luminal subtype A. Luminal subtype A is characterized by a predominant hormone receptor display on immunohistochemical examination. This subtype is a major predictive factor for hormonal therapy and tends to have a better prognosis than other subtypes. HER-2 positive/HER-2 enriched subtype is a subtype with HER-2 positive appearance and hormone receptor negative appearance. This subtype is usually the benchmark in determining the provision of targeting therapy in breast cancer patients. The basal-like/triple negative subtype has an aggressive nature that is thought to stem from the absence of hormone receptors, larger tumor size and higher grading. Patients with this subtype tend to show a shorter survival time. The cause of this poor prognosis remains unclear whether it is due to its aggressive nature or resistance to systemic therapy.¹⁶

CONCLUSIONS

The number of immunohistochemical examinations in breast cancer patients at Mangusada Hospital in 2022-2024 was 182 cases, with the highest age being > 50 years. Diagnosis Invasive Carcinoma of no special type is the most common diagnosis with the most distribution of pathology grading is grade II. The distribution of subtypes based on molecular classification of breast cancer is the luminal B subtype is the most, namely 82 cases, followed by the HER-

2 positive / HER-2 enriched subtype, namely 38 cases, triple negative / basal-like, namely 32 cases and the least is luminal A, namely 28 cases.

CONFLICT OF INTEREST

There are no conflicts of interest in this study.

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AUTHOR CONTRIBUTIONS

All authors have made equal contributions to the writing of this research, from the development of the conceptual framework, data collection, data analysis, to the interpretation of the research results.

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