

# Characteristics and Clinical Description of Breast Cancer Patients in Sanjiwani General Hospital at Gianyar

Pande Made Krisna Ekassiana\*, I Gede Tuban Eling Tulus Widiana  
and I Nyoman Wawan Tirtha Yasa

<sup>1</sup>Division of Oncology at Department General Surgery  
Sanjiwani General Hospital, Gianyar, Bali Indonesia

E-mail: [krisnatogog68@gmail.com](mailto:krisnatogog68@gmail.com); [elinkholic26@gmail.com](mailto:elinkholic26@gmail.com); [nyomanwawan@yahoo.com](mailto:nyomanwawan@yahoo.com)

\*Corresponding author details: Pande Made Krisna Ekassiana; [krisnatogog68@gmail.com](mailto:krisnatogog68@gmail.com)

## ABSTRACT

**Backgrounds:** Breast cancer is the uncontrolled growth of breast cells. The number of new breast cancer cases reached 68,858 cases (16.6%) of the total 396,914 new cancer cases in Indonesia, while the number of deaths reached 22 thousand cases. The rate of breast cancer in Bali ranks first in the most common types of cancer in women. **aim:** Knowing the characteristics and clinical features of breast cancer patients at the Sanjiwani General Hospital in Gianyar from January to December 2021. **Methods:** This study uses a descriptive design to describe or make a description of a condition or situation objectively. This study will use secondary data from medical records at the Sanjiwani Hospital Gianyar, including age, parity, family history, menopausal status, chief complaint, tumor size, metastasis, histopathological type, and breast cancer subtype. Data analysis used univariate data. **Results:** 116 confirmed breast cancer patients mean age  $49.85 \pm 9.89$  years, multipara 75.9%, without a family history, 97.4%, premenopausal and menopause status are the same, most complaints are lumps 45.7%, T4 size 55.2 %, lymph nodes with positive nodules 71.6%, without metastases 91.4%, type Invasive carcinoma of no special type grade 2 38.8%, and luminal subtype B Her 2- 37.9%. **Conclusion:** Most of them are middle-aged, without a family history, with complaints coming because of lumps, T4 size with positive nodules without metastases, most are Invasive carcinoma of no special type grade 2 and subtype Luminal B Her 2 (-).

**Keywords:** breast cancer; breast lump; characteristic; invasive carcinoma; Luminal B

## INTRODUCTION

Breast cancer is the uncontrolled growth of breast cells. Most breast cancers begin in the breast tissue consisting of glands for milk production, called lobules, or in the ducts that connect the lobules to the nipple. Breast cancer can start in the stromal tissue, including the breast's fat and fibrous connective tissue [1]. Based on data from GLOBOCAN (IARC) in 2020, the number of new breast cancer cases reached 68,858 cases (16.6%) of the total 396,914 new cancer cases in Indonesia, while the number of deaths reached 22 thousand cases.[2]

Based on data from Basic Health Research (RISKESDAS) in 2013. Breast cancer affects women, with the second highest prevalence in Indonesia in 2013. Breast cancer was 0.5%. The highest prevalence of breast cancer is in DI Yogyakarta Province, which is 2.4%. Based on the estimated number of breast cancer patients, the highest number is in East Java Province and Central Java Province[3] And based on the 2013 Basic Health Research (RISKERDAS) data, in Bali Province, the estimated number of people with breast cancer was 2,682, the number of providers (program implementers, consisting of general practitioners and midwives) was 53, the number of screenings (an early detection effort to identify diseases or disorders that are not clinically clear by using specific tests, examinations or procedures) was as many as 70,268, and the number of trainers is 6.[4]

Based on research conducted by Diahpradnya et al. from 72 samples of young age (<40 years), grouped by age range, namely <25 years, 25-29 years, 30-34 years, and 35-39 years, the data obtained are breast cancer patients aged young people in 2014-2016 at the age of <25 years were three people (4.1%), aged 25-29 years were five people (7%), aged 30-34 years were 30 people (41.7%), age 35 -39 years old totaling 34 people (47.2%)[5]

According to research Made Satya Wangsa et al., of 253 patients in 2015, the histological picture of invasive ductal carcinoma occupies the highest number, 84.58%, and in 2016 it was 83.54%. Histopathological features of invasive lobular carcinoma in 2015 were 9.10%, and other types of carcinoma were 6.32% of 253 patients. In 2016 of 322 patients, 11.81% had invasive lobular carcinoma histopathology, and 4.65% were different types of carcinoma.[6]

According to research by Komang Trisna Aryawan et al. in 2018 at Sanglah Hospital Denpasar, the highest number of subtypes was triple negative, with patients aged 41-50 years.[7] From these data, it is necessary to conduct research on breast cancer at the Sanjiwani Hospital, Gianyar, to provide public information, education, and counseling.

**METHOD**

This study uses a descriptive design to describe or make a description of a condition or situation objectively. This study will use secondary data from medical records at the Sanjiwani Hospital, Gianyar. The target population is all breast cancer patients at the Sanjiwani Hospital from January 2021 - December 2021. The affordable population of this study is all breast cancer patients who have been histopathologically confirmed at the Sanjiwani Hospital from January 2021 - December 2021.

The inclusion criteria of patients were subjects with breast cancer confirmed by histopathological examination January 2021 - December 2021, and the exclusion criteria

of patients were (a) Having a history of other malignancies, (b) Having a history of immunosuppressive diseases, (c) Incomplete medical records. The analysis was carried out using univariate analysis. The presentation will be distributed in textual and tabular form. Numerical variables are expressed in terms of mean and standard deviation, while categorical variables are defined in frequency and percentage.

**RESULT**

In this study, 116 breast cancer patients were confirmed by histopathological examination from January 2021 - December 2021 at the Sanjiwani Hospital. The characteristics of the distribution data are shown in Table 1.

**TABLE 1:** Characteristics of Research Subjects

Variable	n=116 (%)
<b>Age (Years) mean ± SB</b>	49.85±9.89
<b>Mean parity ± SD</b>	2.21±1.41
Nullipara	18 (15.5)
Primipara	10 (8.6)
Multipara	88 (75.9)
<b>Family history</b>	
There is	3 (2.6)
There aren't any	113 (97.4)
<b>Menopause</b>	
Premenopause	58 (50)
Postmenopause	58 (50)
<b>Main complaint</b>	
Bump	53 (45.7)
Ulcer	41 (35.3)
Bleeding	11 (9.5)
Discharge	11 (9.5)
<b>Tumor size</b>	
T2	20 (17.2)
T3	32 (27.6)
T4	64 (55.2)
<b>Lymph gland</b>	
Negative nodule	33 (28.4)
Positive nodule	83 (71.6)
<b>Metastasis</b>	
Yes	10 (8.6)
Not	106 (91.4)
<b>Histopathological Type</b>	
Invasive lobular carcinoma	10 (8.6)
Invasive carcinoma of no special type grade 1	4 (3.4)
Invasive carcinoma of no special type grade 2	45 (38.8)
Invasive carcinoma of no special type grade 3	44 (37.9)
Invasive micropapillary carcinoma	1 (0.9)
Mixed invasive carcinoma + pleomorphic carcinoma	1 (0.9)
Mixed invasive carcinoma + mucinous carcinoma	1 (0.9)
Ductal carcinoma in situ with micro-invasive focus	1 (0.9)
Solid papillary carcinoma in situ	1 (0.9)
Infiltrating lobular carcinoma	1 (0.9)
Ductal carcinoma in situ	2 (1.7)
Medullary carcinoma	1 (0.9)
Invasive carcinoma grade 1	1 (0.9)
Mixed invasive carcinoma and lobular carcinoma	2 (1.7)
Mixed invasive carcinoma of a special type and lobular carcinoma	1 (0.9)
<b>Subtype</b>	
HER 2 Type	24 (20.7)
Luminal A	3 (2.6)
Luminal B Her 2+	24 (20.7)
Luminal B Her 2-	44 (37.9)
TNBC	16 (13.8)

SD: Standard Deviation

## DISCUSSION

In this study, the results obtained age with a mean  $\pm$  SB  $49.85 \pm 9.89$  years. The risk of breast cancer increases with age. Using the Surveillance, Epidemiology, and End Results (SEER) database, the probability of a woman developing breast cancer is 1 in 8[8]. Both younger and older patients are associated with a poorer prognosis[9]. Patients aged 35 years or younger at diagnosis had a 5-year worse absolute survival than women aged 35 to 69 years (74.7% vs. 83.8%), even after controlling for tumor stage, characteristics, and histopathological factors.[10]. Women >65 also have a poor prognosis, which may be due to a lengthy diagnosis, comorbidities, and less aggressive treatment[11]. The incidence of breast cancer in Bali is not known for sure; 70% of patients are treated at an advanced stage, of which 30-35% are from the childbearing age group under 40 years.[12,13]. The results of the age characteristics at Sanglah Hospital Denpasar in 2009-2013 from 130 subjects with breast cancer obtained the age group > 40 years, namely 77.7%[7]. Meanwhile, in 2014-2016, the results showed that young people <40 years old were around 72 people (14%) out of a total of 514 breast cancer patients, with the highest range being 35-39 years old, which was around 34 people (47.2%).[5].

The number of breast cancer patients was the highest with multipara, namely 88 (75.9%) people with an average of more than two children. 76 times (95% CI 0.80-4.56, p 0.001). This is similar to the risk of breast cancer in multiparas in India, 90.5% with a chance of 2.90 breast cancer, while the data in Indonesia from the Ministry of Health 2020 found 65,858 breast cancer, known to be 89.78% with multipara[2,14,15].

Most of the previous family history was absent, namely 113 (97.4%) people. This is to research by brewer et al. (2017). In 113,000 women with breast cancer in the United Kingdom, it was found that as many as 88,219 (85%) had no previous family history. The risk of breast cancer increased due to a family history of 1.61 times (95% CI 1.35-1.94, P<0.001)[16]. The results of a systematic study also found that only 11.3% of breast cancer cases had a previous family history[17]. In Trisnadewi's research at Sanglah Hospital in 2013, 16 people had a family history of breast cancer and 18 people without a family history, with the risk of family history being eight times (95% CI 1.8-34.8)[18]. The discovery of several members in one family suffering from malignant disease indicates that breast cancer is a familial disease (Li Fraumeni Syndrome/LFS). Women with a family history (in the same lineage) of breast cancer and with atypical hyperplasia (AH) are a high-risk group.[19]. Indrani's research (2012) states that having a family history of breast cancer will increase the risk of breast cancer[20].

The results of menopausal status obtained were the same, namely premenopause and menopause were the same as many as 58 people (50%). The risk of menopause on the incidence of breast cancer has a risk of 3.50 times compared to premenopause[21]. The older a person gets, the more estrogen exposure they experience[22]. The high estrogen level in the breast tissue of postmenopausal women is often ascribed to the increased uptake of circulating hormones that play a role in the high incidence of breast cancer due to hormonal imbalance.[23].

Patients with the most complaints were the presence of a lump in the breast, as many as 53 (45.7%). This is to several studies conducted by Ovaricek et al., 2011; Kamińska et al., 2015; Paalosalo-Harris and Skirton, 2017; Sardanelli et al., 2017 that more than 50% of breast cancer patients complained of by the patient for the first time the presence of an abnormal lump in the breast when touched[17,22,24,25].

In Laisa's research (2017) at Haji Adam Malik General Hospital Medan, 28 people (66.7%) came with complaints of lumps in the breast[26]. According to Suryaningsih and Sukaca (2009), a common symptom of breast cancer is a lump in the breast that can be palpated and usually gets harder, irregular, and sometimes causes pain. Other visible signs, such as changes in shape and size, wrinkles on the skin of the breast so that it looks like an orange peel, and the presence of abnormal fluid in the form of pus, blood, watery fluid, or milk in women who are not pregnant or not breastfeeding that comes out of the nipples. Symptoms of breast cancer generally also appear from swelling in one breast, pulling on the nipple or itchy nipples, and pain. In advanced breast cancer, bone pain, arm swelling, skin ulceration, or weight loss may occur [27].

In this study, the largest tumor size was T4, as many as 64 (55.2%). Tumor size has been recognized as the strongest predictor in patients with invasive breast carcinoma [28]. Tumor size was correlated with the risk of metastases in the axillary lymph nodes, and the 5-year survival was decreased for breast cancer <2 cm (91%), much higher than breast cancer with size > 5 cm (63%)[22,29].

Positive lymph nodes in as many as 83 (71.6%) people. Research Bresser et al. (2010) Of the 220 breast cancer cases, only 55 patients (25%) experienced metastatic axillary lymph nodes based on MRI examination and biopsy results.[30]. Clinically, metastatic axillary lymph nodes will begin to appear in stage IIIA, or III B. 1 KGB with visualized findings based on MRI was 53.7%. Internal mammary lymph node (IMLN) 6% can occur at age <40 years[31]. Study Quetin, Cutuli, and Velten (2001) of 1119 breast cancer cases showed that 10-year survival varied from 30% in patients with positive bilateral axillary lymph nodes to 50% in patients with positive unilateral axillary lymph nodes, compared with 80% in patients with negative axillary lymph nodes.[32].

In this study, the results obtained metastases were found in 106 (91.9%) people. Similar results were found by research Ribnkar et al. 2015 that the incidence of metastases was 10-30% of the overall incidence of breast cancer. Hematogenous and lymphomatous metastases pose a severe threat to breast cancer patients and are responsible for most breast cancer patients' deaths [34,35]. Breast cancer tends to metastasize to specific organs, most commonly the bones, lungs, liver, and brain[36]. It has been reported that 60-70% of breast cancer patients who eventually die are diagnosed with lung metastases[10]. Patients with metastatic breast cancer have a median survival rate of only 22 months after treatment[37].

The most common histopathological type was invasive carcinoma of no special type grade 2 namely 45 (38.8%), and the second most was Invasive carcinoma of no special type grade 3, namely 44 (37.9%) people. This result is different from the research conducted by Diahpradnya (2018) at Sanglah Hospital Denpasar of the 514 patients with the most invasive ductal carcinoma type, namely 61 people (84.7%) while the results in the study of Satya et al. in 2015-2016 found that invasive ductal carcinoma the most, namely 483 (84%) people, invasive lobular carcinoma type as many as 61 people (10.60%)[5,6]. In research, Hartaningsih also found 81.9% with the histopathological classification of invasive ductal carcinoma [38]. Based on a study conducted by Suarfi at Al-Ihsan Hospital Bandung in 2011-2014, from 157 total patients, there were 136 patients with a histopathological type of invasive ductal carcinoma, of which there were 1.27% in patients aged <25 years and 55.41% in 25-50 years old [39].

In a study by Tanriono (2012), the incidence of histopathologic results, namely fibroadenoma, was 62 cases (38.1%). After that, it was followed by invasive ductal carcinoma in 49 patients (30.1%)[40]. This is the same as the research conducted by Suarfi in 2011 at H. Adam Malik Hospital in 2009-2010. The most common benign tumors were fibroadenoma mammae, which was 64 cases (75.3%), while the most common malignant breast tumors were invasive ductal carcinomas, as many as 151 people (77.8%). The most common type of breast cancer is invasive ductal carcinoma, which is 80% of malignant breast cancer tumors [39].

Firdaus' research (2016) proves that histopathological grading will affect the occurrence of molecular subtypes in breast cancer patients. If the molecular subtype is lighter, namely the molecular subtype Luminal A and the molecular subtype Luminal B, the grading is also in excellent and moderate classification, namely grading I and II. On the other hand, if the molecular subtype is Triple Negative, then the grading classification is poor, namely grading III, and the results in this study obtained the most subtype is Luminal B Her 2 (-) as many as 44 (37.9%)[41].

Incidence rates of luminal B breast cancer increased in all age groups for non-Hispanic white women and Asia/Pacific aged 55 to 69 years [42]. Then in a study conducted by Serrano in Colombia, the luminal B breast cancer subtype was the more common subtype (37.2%), followed by luminal A (26.3%), non-basal triple negative (NBTN) (11, 6%), basal like (9%), Human Epidermal growth factor Receptor 2 (HER2) enriched (8.6%) and unknown (7.3%)[43]. In the study of Abubakar et al. et al., from 3,012 patients in Sarawak, Malaysia, Luminal B was ranked second most (33%) after Luminal A (34%), with a death rate in 10 years with a total of 579 patients where Luminal B had the highest number of deaths 150(26%), Luminal A 85(14%), Her-2 type 90(15%), TNBC 110(19%) [44], where research by Widiani et al. stated that based on immunohistochemical examination (IHK), the subtype of breast cancer in Indonesia, Luminal B subtype is the most common compared to other subtypes as many as 544 (43.2%), HER2 subtypes around 214 (17%), TNBC subtypes. 228 (18.1%) were found, and Luminal A subtypes 274 (21.7%) in Bali itself based on Medical Record data at Sanglah Hospital and Peraboi Cancer Registry in 2018-2020 Luminal B subtype breast cancer patients were the most 334 (50.22%), with a mortality rate of 209 (62.5%). Here we conclude that in some western countries, the Luminal A subtype dominates, but in some Asian countries, the Luminal B subtype is increasing in number; then, in Indonesia especially, this subtype has the highest number of patients with increased mortality rates.[45].

In Aryawan's research (2018) at Sanglah Hospital, Denpasar, in 2009-2013, the expected results based on the most immunohistochemical examination subtypes were triple-negative subtypes with the highest incidence rate of 36.9% with the age group 41-50 years being the highest incidence of the total sample of patients. Breast cancer in 2014-2016, the results were obtained with the most subtypes Luminal B (ER+/HER-) and Luminal B HER2 (ER+/HER+) with a total of 31 people (43.1%)[5]. Macdonald et al., from a total of 274 samples of breast cancer patients aged <35 years, it was found that Luminal B subtypes were around 47% and Luminal B/HER2+ were 17%.[46]. Data from the American cancer society suggest that luminal A immunohistochemistry subtypes are found in 40% of breast cancers, luminal B in 10% to 20%, HER2 in 10%, and triple-negative in 10% to 20%. Different findings were also found in a study conducted by Basoli et al. [47].

In this study, the luminal A subtype with the highest incidence was 73.2%, the luminal B subtype was 13.8%, the HER2 subtype was 5.6%, and triple-negative was 7.4% breast cancer in sequence from 1214 samples in this study. However, in a survey conducted in India by Copson et al., the incidence of the triple-negative subtype was relatively high, namely in 25% of the 321 cases sampled.[48]. It is exciting to study the causes of the difference in the highest incidence of breast cancer based on subtypes of immunohistochemical examination in various regions of the world.

## CONCLUSION

Based on the characteristics, it can be concluded that

- (1) The most influencing factor of breast cancer in terms of genetics is age, with a mean  $\pm$  SD 49.85  $\pm$  9.89 years without a family history.
- (2) From premenopausal and postmenopausal hormonal factors, the distribution is the same, and most of them are multiparous.
- (3) Most of the patients complained of an abnormal lump in the breast.
- (4) The tumor size was T4, with positive lymph node condition, and no metastases were found.
- (5) The most common immunohistochemical histopathology was invasive carcinoma of no special type grade 2 and the most subtype is Luminal B Her 2 (-).

## COMPETING INTERESTS

No competing interests were disclosed.

## CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

## ACKNOWLEDGMENTS

declared none.

## ETHICAL APPROVAL

All patient has given permission and informed consent to publish

## REFERENCES

- [1] Nathanson SD, Detmar M, Padera TP, Yates LR, Welch DR, Beadnell TC, et al. Mechanisms of breast cancer metastasis. *Clin Exp Metastasis*. 2021;(0123456789). DOI: 10.1007/s10585-021-10090-2.
- [2] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021;71(3):209-49.
- [3] Riskekdas. *Riset Kesehatan Dasar Nasional*. Riskekdas. 2018;126.
- [4] Riskekdas K. Hasil Utama Riset Kesehatan Dasar (RISKEKSDAS). *J Phys A Math Theor*. 2018;44(8):1-200.
- [5] Diahpradnya Oka Partini P, Nirvana IW, Anda Tusta Adiputra P. Karakteristik kanker payudara usia muda di Subbagian Bedah Onkologi Rumah Sakit Umum Pusat Sanglah tahun 2014-2016. *Intisari Sains Medis*. 2018;9(1):76-9.

- [6] Satya Wangsa IGMSW, Niryana IW, Anda Tusta Adiputra PATA, Pande Arista Dewi NPA. Gambaran stadium dan jenis histopatologi kanker payudara di Subbagian Bedah Onkologi RSUP Sanglah Denpasar tahun 2015-2016. *Intisari Sains Medis*. 2018;9(1):80-4.
- [7] Aryawan ITK. Karakteristik Berdasarkan Pemeriksaan Imunohistokimia Dan Sosiodemografi Pada Penderita Kanker Payudara Di Rumah Sakit Umum Pusat (Rsup) Sanglah Denpasar Tahun 2009-2013. 2018. 2018;7(8):1-6.
- [8] DeSantis CE, Ma J, Gaudet MM, Newman LA, Miller KD, Goding Sauer A, et al. Breast cancer statistics, 2019. *CA Cancer J Clin*. 2019;69(6):438-51.
- [9] Priyatin Cici, Elisa Ulfiana SS. Faktor risiko yang berpengaruh terhadap kejadian kanker payudara DI RSUP Dr. Kariadi Semarang. *J Kebidanan*. 2013;2(5):9-19.
- [10] Song YJ, Shin SH, Cho JS, Park MH, Yoon JH, Jegal YJ. The role of lymphovascular invasion as a prognostic factor in patients with lymph node-positive operable invasive breast cancer. *J Breast Cancer*. 2011;14(3):198-203.
- [11] Zhao X, Qu J, Sun Y, Wang J, Liu X, Wang F, et al. Prognostic significance of tumor-associated macrophages in breast cancer: A meta-analysis of the literature. *Oncotarget*. 2017;8(18):30576-86.
- [12] Narisuari IDAPM, Manuaba IBTW. Prevalensi dan gambaran karakteristik penderita kanker payudara di poliklinik bedah onkologi RSUP Sanglah, Bali, Indonesia tahun 2016. *Intisari Sains Medis*. 2020;11(1):183.
- [13] Saraswati P, Sudarsa I. Kanker Payudara pada Wanita Usia Tua di Rumah Sakit Umum Pusat Sanglah. *E-jurnal Med Udayana*. 2014;3(6):1-9.
- [14] Hinkula M, Pukkala E, Kyryrönen P, Kauppila A. Grand multiparity and the risk of breast cancer: Population-based study in Finland. *Cancer Causes Control*. 2001;12(6):491-500.
- [15] Malvia S, Bagadi SA, Dubey US, Saxena S. Epidemiology of breast cancer in Indian women. *Asia Pac J Clin Oncol*. 2017;13(4):289-95.
- [16] Brewer HR, Jones ME, Schoemaker MJ, Ashworth A, Swerdlow AJ. Family history and risk of breast cancer: an analysis accounting for family structure. *Breast Cancer Res Treat*. 2017;165(1):193-200.
- [17] Paalosalo-Harris K, Skirton H. Mixed method systematic review: The relationship between breast cancer risk perception and health-protective behaviour in women with family history of breast cancer. *J Adv Nurs*. 2017;73(4):760-74.
- [18] Trisnadewi, Sutarga, Duarsa DP. Faktor risiko kanker payudara pada wanita di RSUP Sanglah Denpasar. *Lap Has Penelit Univ Udayana, RSUP Sanglah Denpasar*. 2011;1(2):181-8.
- [19] Zhou W Bin, Xue DQ, Liu XA, Ding Q, Wang S. The influence of family history and histological stratification on breast cancer risk in women with benign breast disease: A meta-analysis. *J Cancer Res Clin Oncol*. 2011;137(7):1053-60.
- [20] Parwati I, Indrati AR, Alam A. Yanti,\* Ida Parwati,\* Agnes Rengga Indrati,\* Anggraini Alam\*\*. 2015;16(5):347-50.
- [21] Sidauruk JTS. Hubungan Usia Dengan Estrogen Receptor Pada Penderita Kanker Payudara di RSUD Dr. Pirngadi Medan Tahun 2018. *Nommensen J Med*. 2020;6(1):1-4.
- [22] Ovcaricek T, Frkovic SG, Matos E, Mozina B, Borstnar S. Triple negative breast cancer - Prognostic factors and survival. *Radiol Oncol*. 2011;45(1):46-52.
- [23] Suparman E, Suparman E. Peran Estrogen Dan Progesteron Terhadap Kanker Payudara. *J Biomedik*. 2014;6(3):141-8.
- [24] Kamińska M, Ciszewski T, Łopacka-Szatan K, Miotła P, Starosławska E. Breast cancer risk factors. *Menopausal Rev*. 2015;3:196-202.
- [25] Sardanelli F, Fallenberg EM, Clauser P, Trimboli RM, Camps-Herrero J, Helbich TH, et al. Mammography: an update of the EUSOBI recommendations on information for women. *Insights Imaging*. 2017;8(1):11-8. DOI: 10.1007/s13244-016-0531-4.
- [26] Laisla. Karakteristik Dan Gambaran Klinis Penderitakanker Payudara Di Rsup Haji Adam Malik Medanperiode Januari – Juni Tahun 2017. 2017;6-8.
- [27] Sukaca, Suryaningsih. Analisis risiko kanker payudara berdasar riwayat pemakaian kontrasepsi hormonal dan usia. *J Berk Epidemiol Vol 3, No 1 Januari 2015* 12-23. 2009;3:12-23.
- [28] Takada M, Toi M. Neoadjuvant treatment for HER2-positive breast cancer. *Chinese Clin Oncol*. 2020;9(3):1-9.
- [29] Abe N, Ohtake T, Saito K, Kumamoto K, Sugino T, Takenoshita S. Clinicopathological significance of lymphangiogenesis detected by immunohistochemistry using D2-40 monoclonal antibody in breast cancer. *Fukushima J Med Sci*. 2016;62(1):57-63.
- [30] de Bresser J, de Vos B, van der Ent F, Hulsewé K. Breast MRI in clinically and mammographically occult breast cancer presenting with an axillary metastasis: A systematic review. *Eur J Surg Oncol*. 2010;36(2):114-9.
- [31] Urano M, Denewar FA, Murai T, Mizutani M, Kitase M, Ohashi K, et al. Internal mammary lymph node metastases in breast cancer: what should radiologists know? *Jpn J Radiol*. 2018;36(11):629-40. DOI: 10.1007/s11604-018-0773-9.
- [32] Quélin P, Cutuli B, Velten M. Lymph node recurrence in breast cancer. Report of 1,119 cases of infiltrating cancer. *Press medicale*. 2001;30(20):996-1000.
- [33] Ribnikar D, Ribeiro JM, Pinto D, Sousa B, Pinto AC, Gomes E, et al. Breast Cancer Under Age 40: a Different Approach. *Current Treatment Options in Oncology*. 2015.
- [34] Ribnikar D, Ribeiro JM, Pinto D, Sousa B, Pinto AC, Gomes E, et al. Breast Cancer Under Age 40: a Different Approach. *Curr Treat Options Oncol*. 2015;16(4).

- [35] Yoon HY, Kim HN, Lee SH, Kim SJ, Chang Y, Ryu S, et al. Association between Neutrophil-to-Lymphocyte Ratio and Gut Microbiota in a Large Population: a Retrospective Cross-Sectional Study. *Sci Rep.* 2018;8(1):1–9. DOI: 10.1038/s41598-018-34398-4.
- [36] Waks AG, Winer EP. Breast Cancer Treatment: A Review. *JAMA - J Am Med Assoc.* 2019;321(3):288–300.
- [37] García-Tejido P, Cabal ML, Fernández IP, Pérez YF. Tumor-infiltrating lymphocytes in triple-negative breast cancer: The future of immune targeting. *Clin Med Insights Oncol.* 2016;10:31–9.
- [38] Hartaningsih, N, M D, Sudarsa I.W. Kanker Payudara pada Wanita Usia Muda di Bagian Bedah Onkologi RSUP Sanglah Denpasar tahun 2002 - 2012. *Garuda J Indones.* 2013;27037:1–14.
- [39] Suarfi AS, Anggraini D, Nurwiyeni N. Gambaran Histopatologi Tumor Ganas Payudara di Laboratorium Patologi Anatomi RSUP M. Djamil Padang Tahun 2017. *Heal Med J.* 2019;1(1):7–14.
- [40] Tanriono S, Rotty LW., Haroen H. Breast Cancer Histopathology for January 2012 - December 2012. *Intern Med Med Fac Univ Sam Ratulangi Manad.* 2012;1–6(December).
- [41] Resti Putri Firdaus V, Asri A, Khambri D, Arif Harahap W. Hubungan Grading Histopatologi dan Infiltrasi Limfovaskular dengan Subtipe Molekuler pada Kanker Payudara Invasif di Bagian Bedah RSUP. Dr. M. Djamil Padang. *J Kesehat Andalas.* 2016;5(1):165–72.
- [42] Acheampong T, Kehm RD, Terry MB, Argov EL, Tehranifar P. Incidence Trends of Breast Cancer Molecular Subtypes by Age and Race/Ethnicity in the US From 2010 to 2016. *JAMA Netw open.* 2020;3(8):e2013226.
- [43] Serrano-Gomez SJ, Sanabria-Salas MC, Hernández-Suarez G, García O, Silva C, Romero A, et al. High prevalence of luminal B breast cancer intrinsic subtype in Colombian women. *Carcinogenesis.* 2016;37(7):669–76.
- [44] Abubakar M, Sung H, Bcr D, Guida J, Tang TS, Pfeiffer RM, et al. Breast cancer risk factors, survival and recurrence, and tumor molecular subtype: Analysis of 3012 women from an indigenous Asian population. *Breast Cancer Res.* 2018;20(1):1–14.
- [45] Ening W. Gambaran Karakteristik Kanker Payudara di RSUP Sanglah Tahun 2014-2015. *Fak Kedokt Univ Udayana.* 2016;4–8.
- [46] Macdonald S, Oncology R, General M. Breast Cancer Breast Cancer. *J R Soc Med.* 2016;70(8):515–7.
- [47] Bassoli S, Ferrari C, Borsari S, Giusti F, Magnoni C, Pellacani G, et al. Negative pigment network identifies a peculiar melanoma subtype and represents a clue to melanoma diagnosis: A dermoscopic study of 401 melanomas. *Acta Derm Venereol.* 2013;93(6):650–5.
- [48] Copson E, Eccles B, Maishman T, Gerty S, Stanton L, Cutress RI, et al. Prospective observational study of breast cancer treatment outcomes for UK women aged 18-40 years at diagnosis: The POSH study. *J Natl Cancer Inst.* 2013;105(13):978–88.