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Adherence to Oral Chemotherapy in Breast Cancer Patients at a Gianyar General Hospital and the Influencing Factors

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ABSTRACT

Background: Breast cancer patients receiving oral chemotherapy must strictly adhere to their treatment regimen for optimal therapeutic outcomes. Various factors, including demographics, environment, social dynamics, and economic circumstances may impact adherence to the recommended treatment.

Objectives: This study aims to assess patient's treatment adherence and decisively identify the factors that affect it.

Methods: This cross-sectional study was conducted at a General Hospital in Gianyar, Bali, in May-June 2024, and 70 samples were purposively selected. Patients with complete medical records and consent were recruited; those with incomplete questionnaires were excluded. An adapted questionnaire and data collection sheet were used to measure adherence and gather medical information. The responses to the adherence questionnaire have been effectively processed into a final scoring format. Higher scores clearly reflect better adherence. Then, the data analysis involved univariate tests to examine respondent characteristics and adherence, as well as bivariate tests (Spearman-rho and Mann Whitney U-Test) to analyze the relationship between respondent characteristics and their adherence (with a 95% CI).

Results: The majority of respondents were <60 years old (75.71%), female (100%), had completed elementary school (28.57%), were employed (64.29%), lived in rural areas (58.57%), had been diagnosed with cancer for <4 years (100%) with stage 3 cancer (47.14%), underwent oral chemotherapy ≤3 times a month (71.43%), had no comorbidities (78.57%), used national health insurance (100%), and had an average adherence score of 88.77±3.72 (moderate of adherence). None of the respondent characteristics mentioned in the results of the respondent description were related to patient adherence (p>0.005).

Conclusion: The patient's adherence to oral chemotherapy is moderate. Other factors suspected to strongly influence better adherence to treatment include consistent treatment monitoring by pharmacists, family support, knowledge, health insurance, and the patient's psychological condition.

Keywords: Adherence; Breast cancer; Oral chemotherapy; Patient's characteristics

INTRODUCTION

In Indonesia, breast cancer is the most prevalent type of cancer in women, following cervical cancer.[1] The Global Cancer Observatory (Globocan) in 2022 by the International Agency for Research on Cancer (IARC) indicated that there were 66,271 new cases of breast cancer, accounting for 30.1% of all new cancer cases in Indonesia, with 22,598 deaths in women, all ages.[2] Provinces, such as Bali, the Special Region of Yogyakarta (DIY), West Sumatra, Gorontalo, and Jakarta, have the highest number of reported breast cancer cases. In 2018, Riskesdas reported that the prevalence of breast cancer in Bali Province was 2.3 cases per thousand, an increase

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from the 2013 figure of 2.0 cases per thousand.[3] The economic impact of breast cancer is significant due to the high costs of treatment. Cancer is the second most expensive health condition after heart disease.[4]

Breast cancer often develops without symptoms, and most patients discover the disease during routine check-ups. Some people may notice lumps in the breast by accident or experience changes in the shape or size of the breast. Additionally, the presence of fluid coming out of the nipple may indicate breast cancer.[5] Recurrence and metastasis of breast cancer cells are the main causes of death from this disease. Treatment options for breast cancer include surgery, radiation therapy, chemotherapy, hormone therapy (endocrine therapy), immunotherapy, and targeted therapy.[6] Chemotherapy plays a crucial role in improving patient survival rates and prognosis.[7] It can be administered before or after other treatments, such as surgery and radiation therapy, to help reduce tumor size. Chemotherapy is also a valuable option when radiation therapy results are unsatisfactory, due to unavoidable treatment delays.[8]

Currently, nearly all breast cancer patients are being treated with oral chemotherapy agents. The use of oral chemotherapy has increased due to various reasons, such as the rising incidence of tumors, patient comfort considerations, the desire to minimize unnecessary medical interventions, and the emergence of significant safety and adherence concerns.[9] Moreover, research by Hanna et al (2021) decisively reviewed multiple studies from around the globe regarding the real-world application of oral chemotherapy in breast cancer patients, and the results demonstrate that globally, many cancer patients greatly prefer oral chemotherapy due to its practicality, reduced toxicity, and lower risk of infection from injection needles.[10] For example, a previous study by Ciruelos et al (2019) in Spain confirmed that approximately 77% of breast cancer patients prefer oral chemotherapy due to its minimal disruption to daily life, ease of administration, and improved adherence to medication schedules.[11]

The survival rate of patients is determined by various factors such as the stage and type of cancer, cancer cell level, receptor status, and overall health. Breast cancer patients need to adhere to chemotherapy to maximize the chances of recovery and achieve optimal therapeutic effects, thus directly impacting their quality of life.[12] Research conducted by Dewi (2020) has demonstrated a significant relationship between chemotherapy adherence and quality of life. The study revealed that patients who adhered to chemotherapy showed a good quality of life (81.8%), while non-adherence patients exhibited a poor quality of life (80%) with a p-value of 0.017.[13] Despite these findings, adherence to chemotherapy remains a major concern in global health. Studies by Bekalu et al (2023) and Onwusah et al (2022) have reported that over 55% of breast cancer patients did not adhere to chemotherapy.[14,15] Various factors influence breast cancer patients' adherence to chemotherapy, encompassing understanding instructions, interactions with healthcare professionals, family support, beliefs, attitudes, and socio-economic factors such as distance, cost, and treatment facilities.[16] Gender, age, place of residence, type of payment, experienced side effects, and the number of chemotherapy drugs obtained also play a role in non-adherence.[14]

Previous studies on patient adherence with oral chemotherapy have primarily used electronic pill caps or questionnaires such as the Morisky Medication Adherence Scale-8 (MMAS-8) to measure general treatment adherence.[14,17,18] This study stands out as it utilizes a specific questionnaire instrument to measure patient adherence to oral chemotherapy.[19] Research on breast cancer patient adherence to oral chemotherapy in Bali Province is still insufficient, especially considering that Bali is one of the regions with the highest breast cancer incidence in Indonesia.[3] According to a 2023 report from the Bali Provincial Health Office, the high number of breast cancer cases in Bali is significantly influenced by the community's low participation in early cancer detection and their fear of the examination results. This reluctance to seek treatment often leads to many new cases being diagnosed at advanced stages.[1] In contrast, previous research conducted by Marangyana et al (2022) focused on the patterns of oral chemotherapy prescriptions in the same area but did not address other important factors, such as patient adherence to treatment.[20] Therefore, this research aims to assess the level of treatment adherence among breast cancer patients undergoing oral chemotherapy using a questionnaire instrument different from the MMAS-8 and to identify the factors influencing patient adherence to oral chemotherapy treatment.

METHODS

Study design

This research is classified as an observational study with a cross-sectional design, where independent and dependent variables are measured simultaneously.[21] The study was conducted at a regional hospital in Gianyar, Bali, from May to June 2024.

Population and samples

The population in this study was 229 individuals with breast cancer who were undergoing oral chemotherapy, which necessitates a minimum sample size of 70 participants to accurately represent the research findings for this population. This calculation is based on Slovin's formula and assumes a margin of error of 10%. The minimum sample size has been verified to meet the study's inclusion and exclusion criteria. Inclusion criteria encompassed patients diagnosed with breast cancer receiving oral chemotherapy, possessing complete medical records, and providing informed consent by completing the necessary documentation. Conversely, individuals who did not fully complete the research questionnaire were excluded from the study.

Study instruments

The research utilized data collection sheets and adherence questionnaires. The adherence questionnaire for oral chemotherapy treatment was based on the EXPAD-ANEO scale questionnaire from a study by Talens et al (2023). This scale was specifically designed to assess adherence with Oral Antineoplastic Agents (OAA) in cancer patients and was adapted to be suitable for the target population. The questionnaire consists of eight dimensions, including 1) treatment experience, 2) polymedication, 3) beliefs about treatment, 4) treatment needs and expectations about effectiveness, 5) information and sources related to treatment, 6) preventing medication errors and ensuring that medications are taken as prescribed, 7) side effects and consequences of treatment with OAA, and 8) social, family, and health professional support, with a total of 20 questions.[19] Since the questionnaire is available only in English, it was translated into Indonesian to accommodate the daily language of the study's respondents. The translation was conducted using the forward-backward translation method at two different language institutions.

Before distributing the questionnaire to various target populations, the researcher conducted a validation and reliability test to ensure the questionnaire's suitability for use in the study. The validity test utilized the construct validity method, specifically using the Pearson Product-Moment correlation formula for each question item in the questionnaire. For the test to be successful, the calculated correlation coefficient (r) value had to be greater than a specified value (r-table). In this case, with 30 trial respondents, the calculated r-value needed to be greater than 0.361.[22] The study also examined the reliability of the questionnaire using the internal consistency method, measured through the Cronbach-alpha value.[23] The results demonstrated that the questionnaire had good validity, with the calculated r-value exceeding the required threshold (0.393-0.803). Furthermore, the reliability test indicated a Cronbach-alpha value of 0.919, confirming that the questionnaire was highly reliable.

Data collection

Data were collected using a questionnaire that had two parts. The first part was a respondent identity sheet, and the second part was a questionnaire to measure respondent adherence to undergoing oral chemotherapy. Additionally, this study also utilized data collection techniques from medical records to verify the respondent's identity and to gather information on the respondent's clinical history.

Data Analysis

The adherence questionnaire comprises 20 questions that respondents must answer using a 5-point Likert scale, ranging from 1 (never) to 5 (always). It's important to note that several questions yield negative responses, except for questions number 2, 6, and 12. In questions that use a negative answer scale, we can simplify data processing by converting the negative responses to a positive scale. Once all the responses to the questions have been standardized on a positive answer scale, the scores for each response are calculated by dividing the respondents' answers by the highest possible score, which is 5, and then multiplying the result by 100. A higher score indicates better adherence to treatment.

To make the data more understandable when describing the samples, adherence is categorized into three levels: poor, moderate, and good. This classification is based on the standard deviation (SD) of the average total respondent score.[24] First, the average adherence score for each respondent is calculated. Next, the overall average adherence score for all respondents is determined, along with the standard deviation. Respondents are then categorized based on their adherence scores: those with scores above the overall average fall into the good adherence category; scores within the average range (±SD) are classified as moderate adherence; and scores below the average (-SD) are classified as poor adherence.

Descriptive analysis of respondent characteristics involves calculating the frequency and percentage of each characteristic. This is achieved by dividing the number of respondents in each group by the total number of respondents and multiplying by 100%. To identify the correlation between respondent characteristics and adherence, bivariate statistical tests are employed. The Spearman-rho test is used for variables with an ordinal-ratio measurement scale, while the Eta test is used for nominal-ratio measurement scale data. However, the Eta test only yields the r-value, so the significance value (p) is obtained using the Mann-Whitney U-test due to the data not being normally distributed (95% confidence level).

RESULTS AND DISCUSSION

Respondent Characteristics

In the study, a sample of 70 female respondents who had been diagnosed with breast cancer for 1-3 years, received national health insurance-covered chemotherapy (specifically, from the Social Security Administering Agency of Health (in Indonesia called BPJS Kesehatan)), and were accompanied by family or close relatives. The sociodemographic characteristics of the respondents indicated that the majority were <60 years old (75.71%), had an elementary school education background (28.57%), were employed (64.29%), and resided in rural areas (58.57%) (see Table I). These findings align with a previous study conducted by Lestari and Lestari (2019) in the Denpasar area, which also reported that most respondents were under 60 years old (51.44%), female (100%), and employed (74.3%), but had a high school/vocational education background (51.3%).[16]

Table I. Respondent Characteristics

Characteristic	n (70)	%
Age (years old)		
< 60	53[a]	75.71
≥ 60	17	24.29
Education level		
No educational background	8	11.43
Elemantary school	20[a]	28.57
Junior high school	17	24.29
Senior high school	14	20.00
High education	11	15.71
Employment status		
Employed	45[a]	64.29
Unemployed	25	35.71
Domicile		
Rural	41[a]	58.57
Urban	29	41.43
Cancer stadium		
1	5	7.14
2	28	40.00
3	33[a]	47.14
4	4	5.71
Frequency of treatment (in a month)		
≤ 3	50[a]	71.43
> 3	20	28.57
Comorbidity		
Yes	15	21.43
1. Diabetes mellitus	4	26.67
2. Hypertension	11	73.33
No	55[a]	78.57

Abbreviation: (a), the highest frequency

According to the resulting study shown in Table I, older age, and gender play a potential role in breast cancer incidence among women. Research from the Lawrence Berkeley National Laboratory indicates that as women age, the cells responsible for maintaining breast tissue lose their ability to respond to signals that suppress tumor growth.[25] Older age is strongly associated with a higher risk of breast cancer, especially in women over 40, due to prolonged exposure to estrogen and other risk factors.[26] Endogenous risk factors, such as early age at first menstruation and later age at menopause, can also increase the risk of breast cancer due to hormonal imbalances.[27] The female gender is associated with an increased risk of breast cancer due to heightened hormonal stimulation, particularly from the hormone estrogen, which can lead to molecular dysfunction by directly altering cell DNA. Estrogen acts as a catalyst for cancer growth by stimulating the division and proliferation of breast tissue, thereby increasing the risk of cancer-causing mutations.[27] Besides that, exogenous risk factors, including alcohol consumption, poor diet, contraceptive pill use, hormone replacement therapy, obesity, sedentary lifestyle, and lack of physical activity, also contribute to the risk of breast cancer. As age increases, the body's cells may become damaged, organ function, such as hormone metabolism in the liver, deteriorates, and the immune system weakens, reducing the body's ability to destroy abnormal cells.[28]

The findings regarding other demographic characteristics, as shown in Table I related to educational background, are discussed in previous studies. Zajacova and Lawrence (2018) reported that women with higher educational attainment generally have better access to health information and a greater awareness of the importance of early breast cancer detection. Education not only increases access to health information and services, but also influences knowledge, attitudes, and behaviors that encourage prevention or early detection of breast cancer, ultimately reducing the burden of cancer in communities.[29] Willems and Bracke (2018) found in their study that individuals with higher education are more likely to seek out cancer screenings on their initiative. In contrast, those with lower levels of education tend to participate in screenings when prompted by a physician or a screening program.[30] Supporting this, Chukwu et al (2024) reported that breast cancer patients with higher education levels generally possess greater knowledge and more positive attitudes toward breast cancer prevention. Well-informed women are more likely to make better decisions regarding their health and well-being.[31]

Employment status and domicile were also described in sociodemographic patients in this study (Table I). Employment status is estimated as a significant factor, as many breast cancer patients continue to work, considering it a sign of recovery and a way to meet their social and economic needs.[32] Peipins et al (2021) found in their study that the majority of breast cancer patients (95%) continued to work after undergoing treatment and recovery. They did so primarily to maintain their health insurance, even though they often experienced reduced working hours, disrupted productivity, or changes in their job status, position, or duties due to their cancer diagnosis, treatment, or related side effects.[33] Andreu et al (2023) in their study also explained that breast cancer patients who are employed experience a positive impact in areas such as financial issues, sexual health, concerns about appearance, social avoidance, and both negative and positive emotions. Being employed is also associated with an improved quality of life (both physically and mentally), especially in terms of common side effects of cancer treatment, like pain and fatigue. They argue that having a job can change how individuals perceive their pain related to cancer and the treatments they are undergoing.[34]

Furthermore, the demographics of a person's residential environment can contribute to the incidence of breast cancer, with residents in rural areas often facing limited access to health services for breast cancer screening and treatment due to the lack of primary and specialist healthcare providers and geographic distance from health facilities.[35] Walji et al (2021) conducted a systematic review and discovered that breast cancer patients in rural areas are more often diagnosed with advanced stages of the disease compared to those in urban areas. It has been shown that a diagnosis at a later stage considerably impacts the mortality rates of breast cancer. Given that cancer screenings help identify the disease before symptoms emerge, such as through precancerous lesions or preclinical stages, the systematic review indicates that differing rates of cancer screening between rural and urban populations could be a significant factor contributing to geographical disparities in cancer outcomes.[36] A study by Bhatia et al (2022) also indicated that disparities in cancer care among rural populations are becoming increasingly recognized and may be deteriorating, potentially due to the effects of living in rural areas on the availability of up-to-date cancer prevention, diagnosis, and treatment services.[37] Acharya et al (2023), in their study, also added that women residing in urban regions are generally more informed about the risk factors associated with breast cancer compared to those in rural areas. They possess a heightened awareness of breast cancer indicators, including breast lumps, nipple discharge, and not breastfeeding. There is a lack of understanding regarding the differences in breast cancer knowledge between women living in urban and rural environments. In rural areas, it has been observed that feelings of shyness and embarrassment during

breast examinations remain prevalent. This suggests that many women struggle to communicate their experiences with healthcare professionals and even their family members, indicating that candid discussions about breast-related issues are not commonplace. Additionally, the absence of a government initiative focused on breast cancer education and screening contributes to a higher likelihood of delayed diagnoses.[38]

Based on the medical history of breast cancer patients undergoing oral chemotherapy, most were in stage 3 (47.14%) with varying treatment frequencies, generally ≤3 times per month (71.43%) and without comorbidities (78.57%) (Table I). A similar study conducted at Sanglah Hospital in Bali showed that the majority of diagnosed patients were mostly in stage 3 (64.06%).[39] The severity of breast cancer is in line with the development of the stages of breast cancer, which is observed based on the size and type of tumor and how many tumor cells have penetrated the breast tissue.[5] In general, the longer breast cancer remains undetected or untreated, the greater the likelihood that the cancer will progress to a more advanced stage.[40] Regarding the frequency of treatment for breast cancer patients undergoing chemotherapy in a month, it varies depending on the stage of the disease and the type of treatment received.[41] In some cases, patients undergoing oral chemotherapy may require scheduling ≤3 times a month or even more than three times. More frequent visits for treatment may be needed to monitor the treatment outcome and manage possible side effects. This also helps to ensure that if serious side effects occur, they can be promptly treated and that dosage adjustments can be made if necessary.[42]

All respondents in this study were treated with a single type of oral chemotherapy called capecitabine. The dosage was adjusted according to recommendations from the Food and Drug Administration (FDA), based on side effects or the doctor's assessment. The treatment cycle was repeated until there was disease progression, unacceptable toxicity, or the patient decided to stop treatment.[43] Breast cancer can impact other organs in the body, leading to varying levels of severity, prognosis, and mortality.[44] In this study, many patients also had comorbidities such as diabetes mellitus (DM) and hypertension. Previous studies have shown that women with type 2 DM have a slightly increased risk of developing breast cancer, possibly due to decreased estrogen levels caused by insulin resistance.[44] Factors such as age, history of early menstruation or late menopause, family history, genetic factors, previous benign tumors, radiation, obesity, oral contraceptives, hormone replacement therapy, and comorbid DM conditions have been identified as risk factors for breast cancer. Additionally, the prevalence of hypertension and breast cancer in women increases with age, and postmenopausal estrogen withdrawal may be a contributing factor to this increase.[45]

The family's support is crucial during oral chemotherapy for breast cancer patients. Strong social support can significantly boost the patient's self-confidence and well-being.[46] It is important for families to provide informational, emotional, and instrumental assistance, as well as empathy, compassion, and appreciation for the patient's accomplishments.[47] Additionally, access to breast cancer care and treatment can be influenced by the patient's payment status or health insurance.[48] Research by Coughlin et al (2020), clearly shows that oncology care can impose a substantial financial burden on patients and their families. This includes costs for medicines, transportation, laboratory tests, and loss of income due to job loss or unplanned retirement.[49] National health insurance plays a critical role in easing this financial burden by covering cancer treatment costs, including surgery, radiation therapy, and chemotherapy for breast cancer.[1]

Respondent Adherence

Adherence is the extent to which patients follow medical recommendations, encompassing their behavior in following therapy instructions.[50] Adherence to oral chemotherapy in breast cancer patients is pivotal for successful therapy and achieving clinical objectives and outcomes related to the patient's quality of life, including physical function, body pain, general health perception, vitality, social function, emotional role, and mental health.[51] Analysis indicates that the majority of respondents have a moderate level of adherence, suggesting that most patients have followed the recommended treatment, although some aspects have not been fully considered or implemented.

According to Table II, the data indicate that the majority of patients exhibit a moderate level of adherence (77.14%) with an average adherence score of 88.98±2.39. A previous study by Wulandari et al (2022), reported similar findings, which showed that 48.7% of colon cancer patients at Tarakan Hospital in Jakarta demonstrated a moderate level of adherence to chemotherapy.[52] In contrast to the research conducted by Jacobs et al (2019), the results showed that most breast cancer patients had poor treatment adherence to oral chemotherapy, particularly among those with high levels of symptom severity.[18] Unal et al (2024) found that 66% of cancer patients reported good adherence to oral chemotherapy.[53] Likewise, research by Mangues-Bafalluy et al (2024)

indicated that over 80% of cancer patients demonstrated good treatment adherence when undergoing oral chemotherapy.[54]

Table II. Overall Adherence to Oral Chemotherapy in Breast Cancer Patients

Variable	Category	n (70)	%	Average ± SD
Adherence	Poor (<85%)	8	11.43	82.13 ± 3.09
	Moderate (85-93%)	54[a]	77.14	88.98 ± 2.39
	Good (>93%)	8	11.43	94.00 ± 1.07
	Total	70	100.00	88.77 ± 3.72

(a), the highest frequency

A challenge of oral chemotherapy is suboptimal adherence due to the lack of routine monitoring and underreporting of symptoms and side effects negatively impacting adherence.[18] Supported Krikorian et al. (2019) found that 90-100% of respondents demonstrated good treatment adherence to their oral chemotherapy. This high level of adherence is likely due to consistent follow-up from healthcare workers, including clinical nurses and pharmacists, who remind patients about their treatment regimens and provide routine education to enhance treatment with oral chemotherapy.[55] However, several significant factors may contribute to non-adherence, including challenges in accessing health services, the advanced stage of cancer, and the patient's perception that doctors overly recommend medications.[53] Furthermore, it was noted that more intense cancer-related symptoms and the adverse effects of oral chemotherapy, including fatigue, drowsiness, sleep problems, memory issues, and emotional distress, played a significant role in reducing treatment adherence. These symptoms were perceived as obstacles that hindered patients from following their treatment plans.[18]

Furthermore, the analysis identifies low adherence in several questionnaire questions, specifically in questions 3, 10, 11, and 13 (Table III). Non-adherence or poor adherence may yield poor clinical outcomes, increased morbidity and mortality rates, and higher healthcare costs.[44] Poor adherence can stem from intentional reasons, such as patient indifference and disbelief in the effectiveness of drugs, as well as unintentional reasons, including forgetfulness and errors in reading drug labels.[13]

Table III. Scoring respondents' adherence per question item

No.	Question	Average ± SD
1	Do you ever miss taking your medication between visits to the pharmacy and hospital?	96.57 ± 8.99
2*	Do you believe that understanding your medications contributes to taking them correctly?	99.14 ± 5.31
3	Have you ever felt like you are taking an excessive amount of medication?	66.57 ± 16.23
4	Do you occasionally cease taking your antineoplastic medication because you believe it is ineffective?	95.14 ± 10.46
5	Have you considered if other Intravena/transplant medications might be more effective than your current oral medication?	87.14 ± 15.98
6*	Do you take your oral medication because you believe the benefits outweigh the drawbacks?	97.14 ± 9.80
7	Have you ever discontinued your medication due to conflicting advice from different healthcare professionals (e.g., primary care physician and specialist (oncologist/hematologist))?	92.57 ± 9.73
8	Have you ever made a dosage or frequency mistake with your oral medication because you thought you were taking too much?	92.57 ± 10.86
9	Have you ever ceased taking your medication because you thought you were taking too much?	89.43 ± 12.61
10	Have your daily activities, including work or leisure activities, ever caused you to forget to take your medication?	68.57 ± 15.06

No.	Question	Average ± SD
11	Do changes in your daily routine (such as having dinner or going for a walk) cause you to forget or miss a dose of your medication?	65.14 ± 11.13
12*	Do you take your oral medication in accordance with the instructions given by your healthcare professional?	99.43 ± 3.36
13	Do you require a family member or friend to remind you to take your medication?	72.57 ± 16.74
14	Have you ever stopped taking your medication because someone else in a similar situation advised you to do so?	96.57 ± 7.54
15	Do you sometimes skip a dose of chemotherapy when you feel unwell?	97.14 ± 7.05
16	Have you stopped taking chemotherapy without consulting your doctor because it drains your energy and makes you tired?	93.14 ± 10.71
17	Have you ever skipped a dose of chemotherapy because you are afraid of reactions such as vomiting, cramps, diarrhea, or skin problems?	89.14 ± 11.64
18	Have you ever halted taking chemotherapy because you were concerned it would affect your work or social life?	89.14 ± 14.32
19	Have you ever stopped taking your medication when you felt well out of fear of becoming sick?	90.86 ± 11.64
20	Have you ever experienced adverse effects with oral medication and required your doctor to prescribe a new medication?	97.43 ± 6.74

(*), questions with a positive answer scale; Note: All scores range from 1 to 100

Question 3 in the questionnaire addresses the patient's feelings when taking too much medication, which may lead to non-adherence. In a study by Kim et al (2019), it was explained that cancer patients undergoing oral chemotherapy may have lower adherence compared to patients undergoing intravenous chemotherapy. This is because they have to take more medication, which can make them feel uncomfortable, anxious, lazy, or even depressed during treatment.[56] Questions 10 and 11 inquire about the patient's daily activities that may cause them to forget to take medication, leading to non-adherence. Research conducted by Jacobs et al (2019) found that over 80% of respondents experienced fatigue and sleep disturbances as side effects of oral chemotherapy treatment.[18] In addition, Dewi (2020) stated in her study that fatigue is one of the most common side effects in cancer patients undergoing oral chemotherapy.[13] It is observed that working and being active in daily activities can exacerbate fatigue and potentially lead to missed medication.[57] Question 13 focuses on the need for support from family or relatives to remind patients to take medication, which can increase patient adherence. Breast cancer patients undergoing oral chemotherapy need support in managing their disease. Family plays a significant role and can provide support in the forms of information, appreciation, emotional assistance, and instrumental help.[46] The support given to patients will aid them in understanding how treatment affects their beliefs, behavior, health, and well-being, influencing their decision-making and potentially improving adherence and therapeutic outcomes.[19]

The Relationship between Respondents Characteristics and Adherence

In Table IV, the study's findings on the relationship between patient characteristics and adherence to oral chemotherapy are unequivocal. None of the characteristics tested exhibited a significant relationship with patient adherence in undergoing chemotherapy ($p>0.05$). These results are further corroborated by previous studies, including one conducted by Jasmine et al. (2022), which revealed no significant relationship between age and adherence in undergoing chemotherapy ($p=0.264$).[58] This finding is attributed to cognitive ability, maturity in thinking, and easy access to health information sources, which neutralize age-related differences in treatment adherence.[59] Another study by Wijaya and Padila (2019) concluded that there is no significant relationship between education level and adherence to chemotherapy ($p=0.728$).[60] While formal education can impact functional ability, cognition, and knowledge, its gradient among patients does not seem to result in different health outcomes.[61] The study emphasizes that formal education alone does not exert a direct influence on behavioral change, highlighting the crucial role of information sources in improving patient adherence to health and treatment recommendations.[60]

In other characteristics, the research by Prihatin et al (2020) found no significant relationship between employment status and adherence in undergoing treatment ($p = 0.872$).[62] This indicates that employment status

does not directly impact treatment adherence, potentially due to the increasing availability of jobs with flexible working hours to promote work-life balance.[48] Likewise, the study by Bekalu et al (2023) definitively shows no significant relationship between place of residence (rural or urban) and adherence to undergoing chemotherapy ($p = 0.76$).[14] This suggests that patients in both rural and urban areas exhibit similar levels of adherence to taking oral chemotherapy drugs. This uniformity in adherence may be attributed to the equitable distribution of health services, widespread public awareness of cancer, consistent government policies, and technological advancements providing equal access to health information for all.[63]

Table IV. The Relationship between Patient Characteristics and Adherence to Oral Chemotherapy

Characteristics (n=70)	Adherence score (average ± SD)	p-value	r-value
Age (years old)			
<60	88.64±3.97	0.581[a]	0.067
≥60	89.18±2.83		
Education level			
No educational background	90.38±1.92	0.280[a]	-0.131
Elemantary school	88.60±3.50		
Junior high school	89.29±3.67		
Senior high school	89.14±2.98		
High education	86.64±5.33		
Employment status			
Employed	89.16±2.90	0.609[c]	0.079[b]
Unemployed	88.56±4.11		
Domicile			
Rural	88.49±3.32	0.142[c]	0.091[b]
Urban	89.17±4.23		
Cancer stadium			
1	86.80±3.70	0.325[a]	0.119
2	86.61±3.19		
3	89.45±4.09		
4	86.75±3.50		
Comorbidity			
Yes	89.47±3.14	0.664[c]	0.107[b]
No	88.55±3.88		

(a) Spearman-rho test; (b) Eta test; (c) Uji *Mann-Whitney U-test*

When studying a patient's medical history, it was found that the stage and history of comorbidities did not have a significant relationship to adherence. This is because awareness of breast cancer and having a strong motivation to recover can help prevent metastasis and tend to make patients more adhere to undergoing treatment.[64] Other clinical conditions, such as the presence or absence of comorbidities, do not affect adherence. Adherence tends to arise from changes in attitude that come from within oneself and from environmental factors such as family support, socioeconomic status, education from health services, adequate health facilities, and sources of information.[65] Although, none of the patient characteristics tested demonstrated a significant relationship to adherence. Therefore, to significantly efforts improve adherence, we can also focus on other factors. This includes consistent monitoring by pharmacists who can remind patients about their treatment regimens and health promotion initiatives that educate patients about cancer conditions and their treatments. Additionally, encouraging patients to routinely self-report their treatment adherence can also be beneficial.[55]

Several limitations may introduce bias into our study. These include the constraints on data collection time leading to a limited sample size and the inability to observe changes in adherence and trends over time. Additionally, the use of a questionnaire in qualitative research, which relies on respondents' understanding, perception, feelings, and memory, can also introduce bias. However, based on the relatively good patient adherence observed, we suggest implementing periodic treatment education by all healthcare professionals,

providing psychological support from family or close relatives to motivate patients, and expanding cancer treatment coverage under national health insurance to alleviate the burden of breast cancer. Furthermore, we recommend combining the assessment of patient adherence with other relevant measurement methods such as patient diaries, Medication Event Monitoring Systems (MEMS), or pill counts to obtain a more comprehensive understanding of adherence.[66]

CONCLUSION

The adherence level of breast cancer patients undergoing oral chemotherapy at a hospital in Gianyar is assessed as moderate (88.77±3.72). There are no significant factors related to patient adherence were found ($p>0.05$). However, it is suspected that factors such as consistent treatment monitoring by pharmacists, family support, health insurance, patient knowledge, and psychological conditions could significantly influence patient adherence.

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None to declare

STATEMENT OF ETHICS

This study was approved by the local Hospital Health Research Ethics Commission under Number 50/PEPK/IV/2024 on May 2, 2024.

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