

Risk Factors for Breast Cancer at Undata Regional General Hospital, Central Sulawesi Province

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Abstract: Breast cancer is one of the most common cancers among women and a growing public health problem, including at Undata Regional General Hospital, Central Sulawesi, where inpatient cases rose from 38 in 2022 to 144 by September 2025. This study aimed to analyze the risk factors associated with breast cancer at Undata Hospital. This is a quantitative study with a case-control design involving 104 respondents (52 cases and 52 controls) selected through purposive sampling. The variables were studied menarche, family history, lactation history, hormonal contraceptive use, and age at first childbirth. Data were analyzed using the Odds Ratio (OR) test in bivariate analysis and multiple logistic regression in multivariate analysis. The results showed that all variables were significantly associated with breast cancer after adjustment: early menarche <12 years (AOR=8.942; 95% CI=1.963–40.740), family history (AOR=13.753; 95% CI=2.973–63.629), lactation duration <12 months (AOR=14.024; 95% CI=4.010–49.045), hormonal contraceptive use ≥5 years (AOR=3.226; 95% CI=1.035–10.060), and age at first childbirth ≥30 years (AOR=9.830; 95% CI=1.703–56.745). The most dominant factor was a lactation duration of less than 12 months. Breast cancer incidence is influenced by an interrelated combination of hormonal, reproductive, and genetic factors, highlighting the need for stronger health promotion, risk-factor education, hormonal contraceptive counseling, and early-detection programs.

Keywords: Risk Factors, Breast Cancer, Menarche, Family History, Hormonal Contraception, Age At Childbirth

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INTRODUCTION

Non-communicable diseases (NCDs) are a serious global health problem. In 2017, NCDs accounted for approximately 74% or approximately 41 million deaths per year globally, increasing to 42 million cases in 2019, and reaching 43.8 million deaths in 2021 (J. Li et al., 2025). According to the WHO Global Health Estimates 2021, cancer ranks second as the cause of death from NCDs after cardiovascular disease, with approximately 9.9 million deaths, with lung, colorectal, liver, gastric, and breast cancers being the types of cancer with the highest mortality rates (J. Li et al.,



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2025).

Globally, cancer accounts for nearly one-sixth (16.8%) of all deaths worldwide and 22.8% of all deaths from non-communicable diseases (NCDs) (Bray et al., 2024). In 2020, breast cancer was the second most commonly diagnosed cancer after lung cancer, with an estimated 2.3 million new cases and 685,000 deaths (Sung et al., 2021), and is projected to increase to 4.4 million cases by 2070 (Lei et al., 2021). Breast cancer accounts for approximately 24.5% of all cancer cases and 15.5% of cancer deaths in women in most countries worldwide (Sung et al., 2021). Based on GLOBOCAN 2022 data, the estimated number of breast cancer cases reached 2.3 million new cases or 11.6% of all cancer diagnoses, with 666,103 deaths in the same year (Bray et al., 2024).

Asia, home to nearly 60% of the world's population, accounts for nearly half of global breast cancer cases, with a higher mortality-to-incidence ratio than Western countries (N. Li et al., 2019). In 2022, an estimated 1 million new cases, or 42.9% of the total global cases diagnosed, are estimated to be in Asia, making breast cancer the most common cancer in women in 43 of the 47 Asian countries (Fu et al., 2025). In Southeast Asia, breast cancer is the most prevalent cancer affecting women across all ASEAN countries, with Singapore having the highest incidence (ASR 72.6 per 100,000 population), followed by the Philippines (60.3), Brunei Darussalam (50.2), Malaysia (46.1), Indonesia (41.8), Vietnam (38.0), and Thailand (37.4) (Christopher et al., 2025). The mortality rate due to breast cancer in Asia reached around 47.3% or around 0.3 million deaths in the same year (Fu et al., 2025).

In Indonesia, cancer is the third leading cause of death after stroke and heart disease. The incidence of breast cancer in women increased from 1.4 per 1,000 in 2013 to 1.79 per 1,000 in 2018 (Ministry of Health of the Republic of Indonesia, 2024). In 2020, breast cancer ranked first with an estimated 68,858 new cases and 22,430 deaths (Sung et al., 2021). GLOBOCAN 2022 data recorded 408,661 new cases and 242,988 deaths from cancer in Indonesia, with breast cancer being the most common cause in women (Ministry of Health of the Republic of Indonesia, 2024). The breast cancer mortality rate in Indonesia also ranks first among 16 other types of cancer, at 14.4 per 100,000 (Fu et al., 2025). The highest prevalence of cancer was found on the island of Java (4.86 per 1,000 population), with the Special Region of Yogyakarta as the province with the highest prevalence of breast cancer, followed by West Sumatra, Bali, DKI Jakarta, and Central Sulawesi (Health Research and Development Agency, 2018).

Breast cancer is a multifactorial disease influenced by the interaction of genetic, hormonal, reproductive, and lifestyle factors (American Cancer Society, 2024). A family history of breast cancer remains a key risk indicator, as the presence of genetic mutations or similar lifestyle patterns in the family can significantly increase an individual's risk (Sung et al., 2021). Biological and reproductive factors also play a significant role; early menarche (<12 years) prolongs the duration of endogenous estrogen exposure in breast tissue, which is correlated with an increased risk of malignancy (Indonesian Ministry of Health, 2018). Having a first child after 30 years of age is also known to increase breast cell vulnerability due to delayed cellular differentiation (American Cancer Society, 2024).

Conversely, a history of lactation has been identified as a protective factor that reduces the risk of breast cancer. A systematic review by Armini et al. (2024) revealed that breastfeeding duration of more than 12 months was consistently associated with a reduced risk of breast cancer. In addition to internal factors, a history of long-term hormonal contraceptive use also plays a role

as an external factor; a recent meta-analysis by Sayon-Orea et al. (2025) showed a linear relationship between duration of hormonal contraceptive use and increased risk of breast cancer, where each additional year of use correlated with a 1% increase in risk; 5–10 years of use increased the risk by 13%, while use of more than 10 years increased the risk by up to 23%.

Epidemiologically, the distribution of breast cancer risk factors varies across regions and social groups in Asia. A meta-analysis by Ang et al. (2024) revealed that Asian women are more susceptible to exogenous hormone exposure from hormonal contraceptives than Western populations. In Indonesia, research by Sukmayenti and Sari (2018) confirmed that reproductive patterns such as short breastfeeding duration and long-term hormonal contraceptive use are dominant determinants that significantly increase the risk of malignancy in the local population.

Mechanistically, most of these risk factors stem from a common biological pathway: the cumulative duration of breast tissue exposure to estrogen throughout a woman's reproductive cycle. Early menarche prolongs the active reproductive phase, resulting in a greater number of menstrual cycles over a lifetime. Delaying first pregnancy until after age 30 prolongs the period when breast epithelial cells are still undifferentiated and therefore more susceptible to carcinogenic stimuli. Long-term use of hormonal contraceptives adds to the exogenous hormonal load through similar mechanisms. Conversely, lactation suppresses ovulation frequency, accelerates terminal differentiation of breast epithelial cells, and promotes exfoliation of cells susceptible to DNA damage. Therefore, longer breastfeeding duration provides a consistent protective effect across populations. Family history complements this picture as a non-hormonal factor associated with the likelihood of inheriting genetic mutations, such as those in the BRCA1 and BRCA2 genes, increases individual susceptibility regardless of reproductive history.

Various previous studies in Indonesia have confirmed the role of these reproductive and hormonal factors, but most remain concentrated in Java, Sumatra, and several other major cities. Analytical data from Eastern Indonesia, including Central Sulawesi Province, remains very limited. This region's sociodemographic characteristics, reproductive patterns, and access to reproductive health services may differ from those in other regions, potentially leading to different patterns of dominant risk factors. This data gap is crucial to address given the consistent upward trend in cases observed in local referral health facilities.

Undata Regional General Hospital (RSUD Undata) is the highest referral hospital in Central Sulawesi Province, playing a key role in the diagnosis and treatment of breast cancer. Medical records show a significant increase in the number of patients from year to year: inpatients with breast cancer increased from 38 cases in 2022 to 85 cases in 2024, and as of September 2025, 144 patients were diagnosed with breast cancer. Similarly, outpatients increased from 108 patients in 2022 to 157 patients in 2024. This increase indicates a shift in risk patterns and predisposing factors in the community. However, analytical research on breast cancer risk factors in Central Sulawesi, particularly at Undata Regional General Hospital as the main referral hospital, is still limited. Understanding risk factors is crucial for strengthening primary prevention programs through risk factor management at the individual and community levels, as well as secondary prevention through strengthening early detection programs such as clinical breast examinations (SADANIS) and screening in high-risk groups. Information on the most dominant risk factors in the local population can also be the basis for formulating evidence-based health policies, both for

hospitals, health services, and health workers in providing education and counseling to patients and the wider community.

Based on the description, this study aims to analyze the risk factors associated with the incidence of breast cancer at Undata Regional General Hospital, Central Sulawesi Province, including menarche, family history, lactation history, history of hormonal contraceptive use, and age at first birth, and to identify the most dominant risk factors associated with the incidence of breast cancer after being controlled by other confounding variables through multivariate analysis.

METHODOLOGY

This study used a quantitative design with a case-control approach to analyze the relationship between independent variables (risk factors) and dependent variables (breast cancer incidence) at Undata Regional General Hospital. Primary data were obtained through structured interviews using a questionnaire, while secondary data were obtained from patient medical records. The study was conducted at the Surgical Oncology Polyclinic and the medical records installation of Undata Regional General Hospital, Central Sulawesi Province, from March to May 2026.

The case population consisted of all 271 female patients diagnosed with breast cancer at Undata Regional General Hospital between January 1, 2024 and June 30, 2025, who underwent outpatient treatment at the Surgical Oncology clinic. The control population consisted of women not diagnosed with breast cancer at the same clinic. The sample size was calculated using the Lemeshow formula based on family history variables, resulting in a minimum sample size of 94 respondents (47 cases and 47 controls); with an additional 10% to anticipate incomplete data, the total sample size was set at 104 respondents (52 cases and 52 controls). The sampling technique used non-probability sampling with a purposive sampling method—consecutive sampling for the case group and a 1:1 ratio for the control group.

The inclusion criteria for the case group included female patients diagnosed with breast cancer clinically and histopathologically (ICD-10 C50) with complete medical records, aged 20–65 years and married, willing to be respondents and sign informed consent, and able to communicate well. The inclusion criteria for the control group included female patients treated at Undata Regional General Hospital without a diagnosis of breast cancer and with baseline characteristics comparable to the case group. Exclusion criteria included patients with other comorbidities and those who refused to participate.

The variables studied included menarche (early <12 years vs normal ≥ 12 years), family history (presence/absence of breast cancer in the immediate family), lactation history (breastfeeding duration <12 months vs ≥ 12 months), history of hormonal contraceptive use (≥ 5 years vs <5 years), and age at first birth (≥ 30 years vs <30 years), all measured through questionnaire-based interviews that had been tested for validity and reliability.

Data analysis was performed using the SPSS program in three stages. Univariate analysis was used to describe the frequency distribution and percentage of each variable. Bivariate analysis used the Chi-Square test to determine the significance of the relationship between variables ($p < 0.05$) and was continued with the calculation of the Odds Ratio (OR) along with the 95% Confidence Interval (CI) to measure the strength of the association. Multivariate analysis used binary logistic regression to determine the most dominant risk factors after controlling for

confounding variables, resulting in an Adjusted Odds Ratio (AOR) value; a variable is declared a confounder if its removal from the model changes the OR value of the main variable by $\geq 10\%$. Bias control was carried out through the application of strict inclusion-exclusion criteria, age matching between case and control groups, standardization of research instruments, training of enumerators, and data objectification by matching interview results with medical records.

RESULTS AND DISCUSSION

Respondent Characteristics

This study involved 104 respondents, consisting of 52 cases and 52 controls. Respondent characteristics based on age, education, and occupation are presented in Table 1.

Table 1. Respondent Characteristics (n=104)

Characteristics	f	%
Age		
20–39 years	28	26.9
40–50 years	26	25.0
51–65 years	41	39.4
66–70 years	9	8.7
Education		
Elementary School	4	3.8
JUNIOR HIGH SCHOOL	27	26.0
SENIOR HIGH SCHOOL	36	34.6
Diploma III	7	6.7
S1	28	26.9
S2	2	1.9
Work		
Housewife	68	65.4
Private	7	6.7
Honorary	5	4.8
Teacher	1	1.0
ASN	23	22.1
Total	104	100

Source: Primary Data, 2026

The majority of respondents were in the 51–65 age group (39.4%), had a high school education (34.6%), and were housewives (65.4%). This distribution indicates that the majority of respondents were in the age group at higher risk for breast cancer.

Univariate Analysis

The frequency distribution of the five research variables in the case and control groups is presented in Table 2.

Table 2. Distribution of Research Variables in Case and Control Groups

Variables	Case (f)	Case (%)	Control (f)	Control (%)
Menarche				
Early (<12 years)	12	23.1	3	5.8
Normal ($\geq$ 12 years)	40	76.9	49	94.2
Family history				
There is a history	17	32.7	3	5.8
No history	35	67.3	49	94.2
Lactation history				
Duration <12 months	26	50.0	7	13.5
Duration $\geq$ 12 months	26	50.0	45	86.5
Hormonal contraception				
Use $\geq$ 5 years	31	59.6	27	51.9
Use <5 years	21	40.4	25	48.1
Age at first birth				
$\geq$ 30 years	10	19.2	3	5.8
<30 years	42	80.8	49	94.2

Source: Primary Data, 2026

Across all variables, the proportion of exposure to risk factors (early menarche, family history, short duration of lactation, use of hormonal contraception $\geq$ 5 years, and age at first birth $\geq$ 30 years) was consistently higher in the case group than in the control group, with the most striking differences in proportions seen in the family history and lactation history variables.

Bivariate Analysis

The results of the Chi-Square test and Odds Ratio (OR) calculations for each variable are presented in Table 3.

Table 3. Results of Bivariate Analysis of Risk Factors for Breast Cancer Incidence

Variables	OR	95% CI	p
Early menarche (<12 years)	4,900	1,293–18,570	0.021
Family history	7,933	2,158–29,161	0.001

Lactation history <12 months	6,429	2,451–16,860	<0.001
Hormonal contraception ≥5 years	1,367	0.629–2.971	0.430
Age of first birth ≥30 years	3,889	1,004–15,068	0.049

Source: Primary Data, 2026

In the bivariate analysis, four of the five variables showed a statistically significant association (95% CI value did not exceed 1), namely early menarche (OR=4.900), family history (OR=7.933), history of lactation <12 months (OR=6.429), and age at first birth ≥30 years (OR=3.889). The variable history of hormonal contraceptive use ≥5 years did not show a statistically significant association (OR=1.367; 95% CI=0.629–2.971; p=0.430), but was retained in the multivariate model due to its strong theoretical basis and epidemiological evidence from previous studies.

Multivariate Analysis

All variables that met both bivariate and theoretical criteria were entered into a multiple logistic regression model. A confounding test showed that all variables caused a ≥10% change in the OR of the primary variable (lactation history) when removed individually, resulting in the final full model. The results of the multivariate analysis are presented in Table 4.

Table 4. Results of Multivariate Analysis (Multiple Logistic Regression)

Variables	p-value	AOR	95% CI Lower	95% CI Upper
Menarche	0.005	8,942	1,963	40,740
Family history	<0.001	13,753	2,973	63,629
Hormonal contraception	0.044	3,226	1,035	10,060
Age at first birth	0.011	9,830	1,703	56,745
Lactation history	<0.001	14,024	4,010	49,045

Source: Primary Data, 2026

The results of the multivariate analysis showed that all five variables remained statistically significantly associated with breast cancer incidence after mutual control. Lactation history with breastfeeding duration <12 months was the most dominant independent risk factor (AOR=14.024; 95% CI=4.010–49.045; p<0.001), followed by family history (AOR=13.753), age at first birth ≥30 years (AOR=9.830), early menarche (AOR=8.942), and use of hormonal contraception ≥5 years (AOR=3.226).

Menarche and Breast Cancer Incidence

Early menarche causes exposure to endogenous estrogen hormones to occur earlier and last longer throughout reproductive life, thereby increasing the stimulation of breast epithelial cell proliferation and the risk of genetic mutations (Khuzaiyah, 2024). In this study, the proportion of

early menarche was significantly higher in the case group (23.1%) compared to the control group (5.8%), with the risk increasing from 4.9 times in bivariate analysis to almost 9 times in multivariate analysis (AOR=8.942), confirming early menarche as an independent risk factor. This finding is in line with research by Rahmatia (2024), Lubis (2023), and Agussalim (2024) which also reported an association between younger age at menarche and increased incidence of breast cancer due to longer duration of estrogen exposure (Marlia, 2024; Pringsewu et al., 2023). However, several studies such as Aulia (2025) and Sukma (2022) reported insignificant results after controlling for other reproductive factors, which was likely due to differences in respondent characteristics and confounding factors that were not fully controlled.

Family History and Breast Cancer Incidence

Family history is a non-modifiable risk factor because it is associated with the possibility of inheriting genetic mutations, particularly the BRCA1 and BRCA2 genes (Wang et al., 2023). This study found that respondents with a family history of breast cancer had a 7.9-fold greater risk in bivariate analysis and increased to 13.8-fold in multivariate analysis (AOR=13.753), making it the second strongest independent risk factor after lactation history. These results are consistent with Wang et al.'s (2023) systematic review in Asian populations, as well as studies by Yolanda (2023) and Suanjaya et al. (2025), which also found a strong association between family history and breast cancer incidence. In contrast, Firman's (2022) study found no significant association, suggesting that lifestyle and hormonal factors are more dominant than genetic factors in this population.

Lactation History and Breast Cancer Incidence

Breastfeeding provides a protective effect by suppressing ovulation frequency, terminal differentiation of breast epithelial cells, and exfoliating cells that are potentially exposed to DNA damage at the end of lactation (Obeagu, 2024). This study shows that lactation history is the most dominant risk factor associated with breast cancer incidence at Undata Regional General Hospital; respondents with a breastfeeding duration of <12 months had a 6.4-fold greater risk in bivariate analysis and 14-fold greater risk in multivariate analysis (AOR=14.024) compared to respondents who breastfed ≥ 12 months. This finding is in line with the systematic review by Armini et al. (2024) and the study by Wandari (2025) which showed a consistent protective effect of breastfeeding on breast cancer risk. However, studies by Marlita (2025) and Herita (2024) did not find a significant association, indicating that the effect of lactation on breast cancer may vary in each population depending on other accompanying reproductive and genetic factors.

Hormonal Contraceptive Use and Breast Cancer Incidence

Hormonal contraceptives contain synthetic estrogen and progesterone, which can stimulate the proliferation of breast epithelial cells when used long-term (Sayon-Orea et al., 2025). In bivariate analysis, the association between hormonal contraceptive use for ≥ 5 years and breast cancer incidence was not statistically significant (OR=1.367; $p=0.430$), but became significant after being controlled for other variables in multivariate analysis (AOR=3.226; $p=0.044$), indicating that the effect of hormonal contraception on breast cancer risk needs to be understood in conjunction with other reproductive factors. This finding is in line with the meta-analysis by Sayon-Orea et al. (2025) and the study by Fitzpatrick et al. (2023) which showed an increasing

risk of breast cancer with increasing duration of hormonal contraceptive use, as well as studies by Sulaeman (2021) and Hassan (2025) in more limited populations.

Age at First Birth and Breast Cancer Incidence

Women who give birth to their first child at a young age experience earlier differentiation of breast epithelial cells, making breast tissue more resistant to carcinogenic stimuli, while delaying pregnancy prolongs the period of estrogen exposure before complete differentiation occurs (Denny et al., 2022). This study found that age at first birth ≥ 30 years increased the risk of breast cancer by 3.9 times in bivariate analysis and 9.8 times in multivariate analysis (AOR=9.830), making it a strong independent risk factor. These results are consistent with research by Meylissa and Lestari (2024) at Dr. Zainoel Abidin Regional General Hospital, Banda Aceh, as well as Prazeris (2023) and Qhotrunnada (2023), which also reported an increased risk of breast cancer in women with an older age at first birth.

Research Limitations

This study has several limitations. First, the collection of reproductive and hormonal history data through interviews has the potential to introduce recall bias, particularly for variables that occurred decades earlier, such as age at menarche and age at first birth. Second, the case-control design with a relatively short study period did not allow for longitudinal observation of changes in risk factors. Third, the variables studied were limited to five reproductive and genetic factors, while other factors such as obesity, diet, physical activity, alcohol consumption, and smoking have not been studied in depth. Fourth, this study was conducted only at a single institution (Undata Regional General Hospital), so generalization of the results to other areas in Central Sulawesi requires caution... Fifth, several adjusted odds ratios in the multivariate model showed very wide 95% confidence intervals (e.g., lactation history AOR=14.024, 95% CI=4.010–49.045; family history AOR=13.753, 95% CI=2.973–63.629; age at first birth AOR=9.830, 95% CI=1.703–56.745), occurring alongside very small cell counts in several exposure categories among controls (e.g., only 3 controls with a family history and only 3 controls with early menarche, out of 52). This combination of wide intervals and sparse cells is consistent with sparse-data bias or quasi-complete separation in the logistic regression model, which can inflate point estimates and destabilize confidence intervals. Consequently, the magnitude of these associations, particularly the reported 13–14-fold increases in risk, should be interpreted with caution rather than as precise effect estimates. Future studies with larger samples, or the use of penalized regression methods such as Firth's correction, are recommended to obtain more stable and reliable estimates.

CONCLUSIONS

This study concluded that early menarche (<12 years), family history of breast cancer, history of lactation with breastfeeding duration <12 months, use of hormonal contraception ≥ 5 years, and age at first birth ≥ 30 years were risk factors significantly associated with breast cancer incidence in Undata Regional General Hospital, Central Sulawesi Province after being controlled by other confounding variables. History of lactation with breastfeeding duration less than 12 months was the most dominant risk factor (AOR=14.024; 95% CI=4.010–49.045), followed by family history (AOR=13.753), age at first birth (AOR=9.830), early menarche (AOR=8.942), and use of hormonal contraception (AOR=3.226). These findings confirm that breast cancer incidence

is influenced by a combination of interrelated hormonal, reproductive, and genetic factors. Healthcare workers and hospital institutions are expected to strengthen the promotion of exclusive breastfeeding, education on reproductive risk factors, counseling on the safe use of hormonal contraception, and early detection programs such as clinical breast examinations (SADANIS) and screening for high-risk women to reduce breast cancer incidence in Central Sulawesi. Future research is recommended to examine additional risk factors such as obesity, diet, physical activity, and specific genetic factors with a larger sample size and broader coverage area.

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