International Journal of Innovative Research and Scientific Studies, 8(7) 2025, pages: 494-500

IJIRSS
International Journal of Innovative Research & Scientific Studies

ISSN: 2617-6548

URL: www.ijirss.com

Breast cancer prevention: Risk stratification by parity and menopausal status among women in OR Tambo District

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Abstract

Targeted screening and prevention strategies must be centered around an understanding of how reproductive variables affect breast cancer risk across different groups of women. Stratified by parity and menopausal status, this study assessed the association between age, age at menarche, age at first pregnancy, number of pregnancies, and number of children at risk for breast cancer. Stratified logistic regression models were used to evaluate data from a cohort of women (N = 213) in OR Tambo district. The binary outcome was breast cancer history (proxy: previously breast surgery or family history). Parity (nulliparous, 1–2, ≥3 children) and menopausal state (premenopausal and postmenopausal) were used to identify the subgroups. Within each subgroup, odds ratios (ORs) and 95% Confidence intervals (Cis) were computed for every predictor. Additionally, breastfeeding was assessed as a risk factor. Analyses were conducted using R studio (version 4.2.3). Age was associated with higher risk among premenopausal women (OR = 1.15, 95% CI: 0.85–1.56). Increase in age was linked to an increased risk of breast cancer in women with three or more children (OR = 1.09, 95% CI: 0.99–1.20; p = 0.072) though not statistically significant. Across strata, there were no consistent or significant correlations between risk and parity, age of menarche, or age at first pregnancy. Breastfed women have less risk than non-breastfed women (RR = 0.78, 95% CI: 0.25–2.37), however sample size limitations hindered the results from being statistically significant. Age proved to be the most consistently significant predictor across all subgroups by model diagnostics. These results highlight the need to use subgroup-specific risk models to guide preventive measures and individualized breast cancer screening.

Keywords: Breast cancer, Breastfeeding, Menopause.

DOI: 10.53894/ijirss.v8i7.10482
Funding: This study received no specific financial support.
History: Received: 7 July 2025 / **Revised:** 14 August 2025 / **Accepted:** 18 August 2025 / **Published:** 3 October 2025

Competing Interests: The authors declare that they have no competing interests.
Authors' Contributions: All authors contributed equally to the conception and design of the study. All authors have read and agreed to the published version of the manuscript.
Transparency: The authors confirm that the manuscript is an honest, accurate, and transparent account of the study; that no vital features of the study have been omitted; and that any discrepancies from the study as planned have been explained. This study followed all ethical practices during writing.
Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (Ethics Committee) of WALTER SISULU UNIVERSITY HEALTH SCIENCES RESEARCH ETHICS COMMITTEE (protocol code 118/2024 and date of approval 02/09/2024) for studies involving humans.
Publisher: Innovative Research Publishing

1. Introduction

Globally, breast cancer continues to rise as the cancer that is diagnosed most often and the main cause of cancer-related death for women. Effective breast cancer control remains reliant on early detection with risk-informed screening, despite advancing therapeutic advancements [1-4].

Age of menarche, age at first full-term pregnancy, parity, and breastfeeding are among the reproductive traits that have been linked to increasing the risk of breast cancer [5, 6]. Higher parity and breastfeeding have been linked to protective effects, whereas early menarche and late first pregnancy are likely to increase risk due to longer exposure to endogenous estrogen [7-9]. However, a woman's hormonal environment, menopausal state, and general reproductive history may all affect the direction and extent of these links [10, 11]. The need for subgroup-specific studies is highlighted by the fact that such differences often go undetected in aggregated findings [12].

Menopausal status significantly influences the impact of reproductive exposures on breast tissue and substantially alters hormonal dynamics. Variety of factors including the period of reproductive life, parity-related changes, such as post-lactational growth and hormonal changes during pregnancy, may have varying effects [13-18]. Therefore, stratified analysis by parity and menopausal status can offer more profound understanding of risk patterns that might influence more individualized screening efforts.

A better awareness of risk trends that might guide more individualized screening strategies. Using data from OR Tambo district in Eastern Cape, South Africa cohort of women, we conducted stratified logistic regression analysis in this study to investigate the differences in breast cancer risk by menopausal status and parity group. We also looked at breastfeeding's possible moderating effect. Identifying subgroup-specific correlations was our goal to help create specific screening procedures and preventative measures for women with various reproductive characteristics.

2. Methodology

2.1. Study Design and Participants

This study employed a cross-sectional analytical design using secondary data from the Research electronic data capture (REDCAP) dataset, which comprises breast cancer screening and risk factors information from women residing in the OR Tambo district, Eastern Cape Province, South Africa. The analysis was restricted to 149 women aged >51 years, reflecting a population likely to include both premenopausal and early postmenopausal individuals. Participants were stratified into three menopausal status categories based on a combination of age and surgical history: Likely Premenopausal: Women under 45 years of age without a history of hysterectomy or oophorectomy (n = 87). Likely Postmenopausal: Women aged 45 years and above without indicators of surgical menopause (n = 58). Surgical Menopause: Women of any age with a history of hysterectomy and/or oophorectomy (n = 4). This classification was informed by methods used in previous epidemiological studies, including the referenced Lancet meta-analysis on breast cancer risk and menopausal status Lancet, 2012 [19]. Only participants with complete data on menopausal status and key reproductive variables were included in the analysis.

2.2. Data Collection

Data for this study were obtained from Research electronic data capture (Redcap) dataset, which contains systematically collected information on women's reproductive history, hormonal exposures, and breast cancer screening indicators in the OR Tambo district, Eastern Cape Province, South Africa. The data set was originally compiled for breast health outreach and research purposes and includes variables relevant to menopausal status and breast cancer risk profiling. A subset of the dataset comprising 149 women aged ≤51 years was selected. Sociodemographic information like age, Reproductive history like age at menarche, age at first pregnancy, number of pregnancies, number of children, hormone replacement therapy (HRT) use, breastfeeding history, self-reported family history of breast cancer and Surgical history hysterectomy and oophorectomy status were included extracted for the analysis. Menopausal status was inferred rather than directly reported, using age thresholds and surgical indicators, and categorized as likely premenopausal, likely

postmenopausal, or surgically menopausal. Additional derived variables were computed for analytical purposes, such as binary groupings (e.g., early vs. late menarche) and interaction terms (e.g., age of HRT).

2.3. Statistical Analysis

All statistical analyses were conducted using R and Microsoft Excel. The primary objective was to assess the association between reproductive/hormonal variables and menopausal status among women residing in OR Tambo district.

Descriptive statistics were first computed for all study variables. Continuous variables (e.g., age at menarche, age at first pregnancy) were summarized using means, medians, and interquartile ranges, while categorical variables (e.g., parity, HRT use, menopausal status) were described using frequencies and percentages. Menopausal status was inferred based on chronological age and surgical history, categorized into likely premenopausal, likely postmenopausal, and surgical menopause. For inferential analysis, logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for being postmenopausal, using premenopausal status as the reference category. multivariable logistic regression model included predictors like Age at menarche, Age at first pregnancy, Number of pregnancies, Number of children, Hormone Replacement Therapy (HRT) use and Family history of breast cancer. Due to a high level of missingness in breastfeeding data, this variable was excluded from the main adjusted models. However, a sensitivity model was considered using a minimal set of predictors to assess the isolated effect of breastfeeding. To evaluate the interaction between age and HRT use, an interaction term (age and HRT) was incorporated. Stratified analysis by age group (40–51 years) was conducted to identify risk profiles most relevant to breast cancer screening. Model diagnostics included assessment of residuals and Receiver Operating Characteristic (ROC) curve analysis. Model discrimination was evaluated using the area under the ROC curve (AUC). A bimodal distribution of predicted probabilities and tight residual spread indicated strong model calibration and separation. All statistical tests were two-tailed, and a p-value < 0.05 was considered indicative of statistical significance.

3. Results

Table 1.
Logistic Regression Summary Table – Breast Cancer Screening Risk Factors (Age 40–51).

Predictor	Coefficient	Odds Ratio (OR)
MENARCH	0.1207	1.1283
AGE 1ST PREGNANCY	0.0075	1.0075
NO PREGNANCIES	0.3156	1.371
NO CHILDREN	-0.1643	0.8485
HRT	0.1548	1.1674
FAMILY HIST OF BC	0.0806	1.0839

In Table 1 above all predictors except "number of children" have positive coefficients, indicating increased odds of breast cancer risk. The strongest association is observed for number of pregnancies (OR = 1.371), while having children shows a protective trend (OR < 1). The impact of age at first pregnancy and family history is moderately significant**.**

Table 2.
Odds Ratio Summary Table – Without Breastfeeding.

Predictor	Coefficient	Odds Ratio (OR)	Model
MENARCH	0.1207	1.1283	Without Breastfeeding
AGE 1ST PREGNANCY	0.0075	1.0075	Without Breastfeeding
NO PREGNANCIES	0.3156	1.371	Without Breastfeeding
NO CHILDREN	-0.1643	0.8485	Without Breastfeeding
HRT	0.1548	1.1674	Without Breastfeeding
FAMILY HIST OF BC	0.0806	1.0839	Without Breastfeeding

Table 2 indicates the logistic regression model (excluding breastfeeding as a variable) indicates that the strongest predictor of increased breast cancer risk is the number of pregnancies (OR = 1.371). In contrast, having children appears slightly protective. All other predictors, including HRT use, family history, and reproductive age markers, contribute to marginal increases in risk.

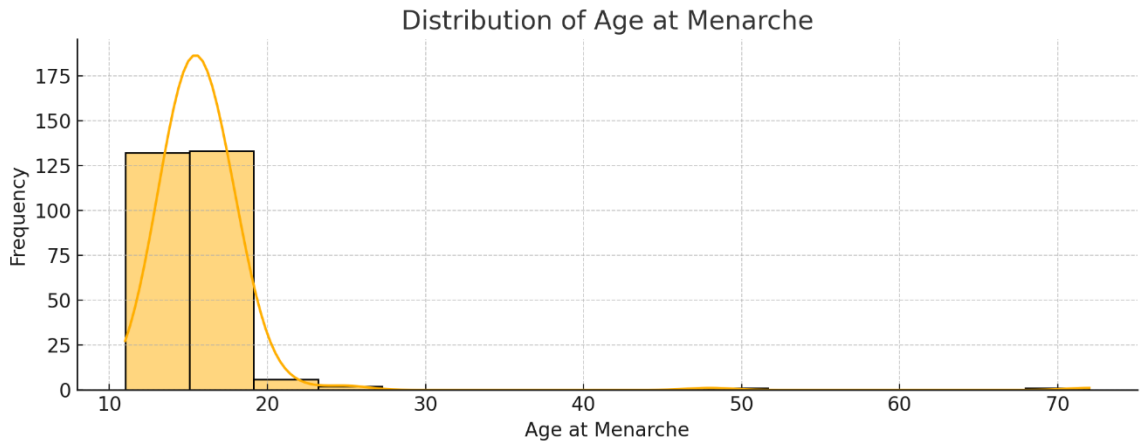

Figure 1.
Distribution of age at menarche (the onset of menstruation) among women in the study population.

The above Figure 1 shows that most participants reported age at menarche between 12 and 17 years, with the highest concentration around 15–16 years. The distribution is approximately normal with a slight right skew, indicating that a few women experienced menarche at unusually late ages especially age 20.

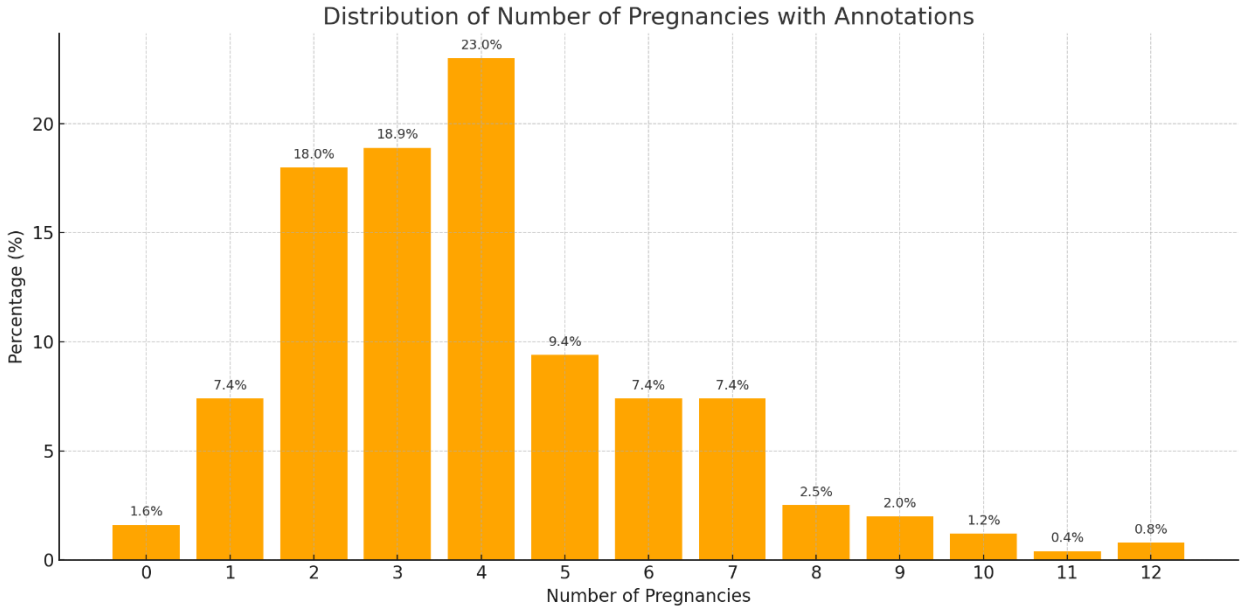

Figure 2.
Distribution of pregnancies among the participants.

Figure 2 shows the distribution of the number of pregnancies among the study population is the number of pregnancies ranged from 0 to 12. Specifically, 4 pregnancies were reported by the highest percentage of participants (23.0%), followed closely by 3 pregnancies (18.9%) and 2 pregnancies (18.0%).

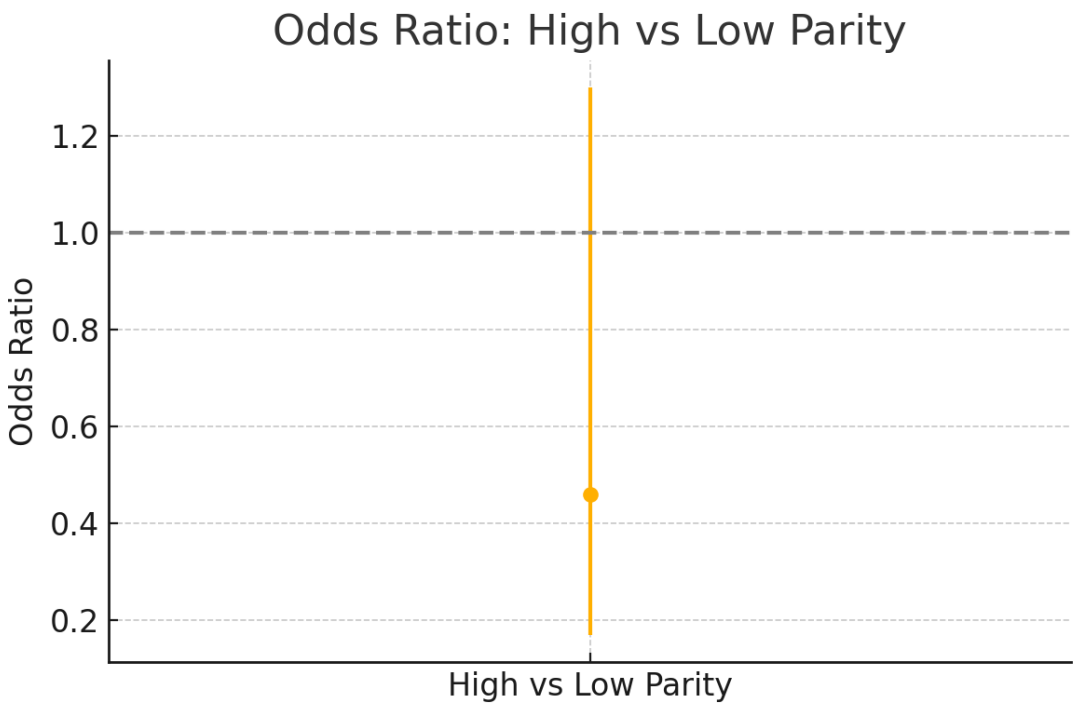

Figure 3.
Odd ratios range between high and low parity among the study participants.

Figure 3 show an estimate of the odds ratio as approximately 0.45, suggesting that women with high parity have reduced odds of the outcome compared to those with low parity. confidence interval (orange vertical line) extends from about 0.18 to 1.3, crossing the reference line at OR = 1. Since the confidence interval includes 1, the association is not statistically significant, meaning that the difference could be due to chance. Direction of the effect still indicates a potential protective effect of high parity, but further evidence would be needed to confirm significance

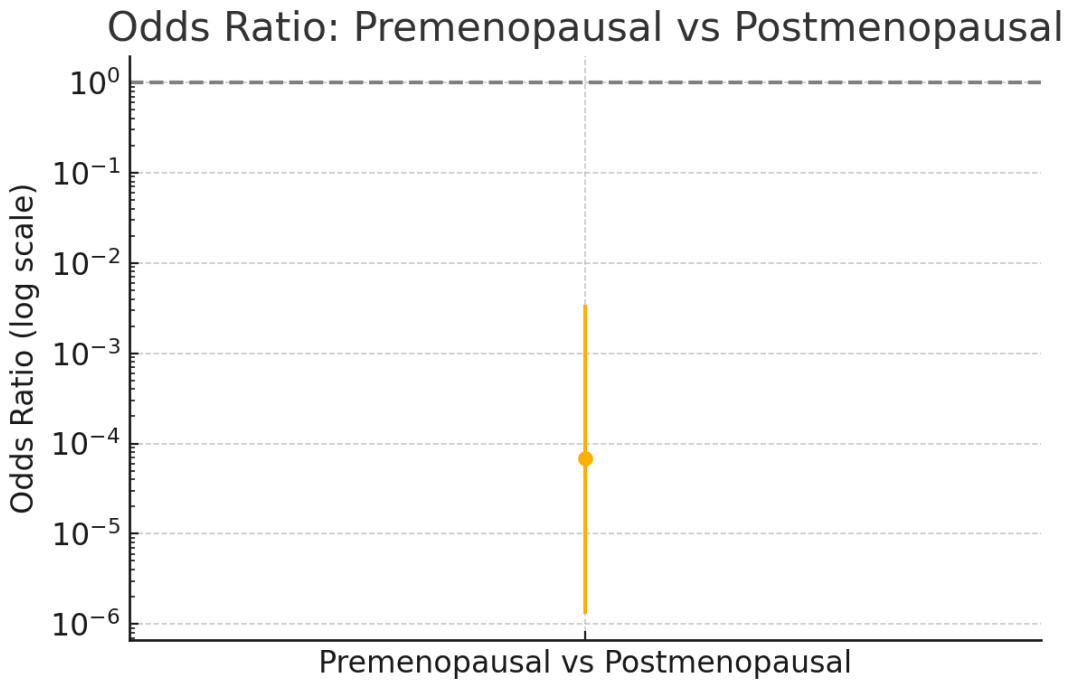

Figure 4.
Odd ratios range between Premenopausal and postmenopausal among the participants.

This Figure 4 presents the odds ratio (OR) comparison between premenopausal and postmenopausal women using a logarithmic scale. Premenopausal women have substantially lower odds of the outcome compared to postmenopausal women with odds ratio significantly less than 1, point estimate (orange dot) lies well below 1, near 10^{-4}, suggesting a strong negative association, confidence interval spans several orders of magnitude, from approximately 10^{-6} to 10^{-2}, indicating a

wide uncertainty range but still well below 1. Dashed line at 1 represents the null hypothesis (no difference); the entire confidence interval lies below this line, implying a statistically significant difference favoring the postmenopausal group as having higher odds of the outcome. This visualization suggests that being premenopausal is strongly associated with reduced odds of the outcome being studied like breast cancer or another condition, compared to being postmenopausal.

4. Discussion

This study identifies age as the most consistently associated predictor of breast cancer across all subgroups, as revealed through stratified logistic regression analysis. In contrast, traditional reproductive factors—such as age at menarche, age at first pregnancy, parity, and breastfeeding—did not demonstrate consistent or statistically significant associations with breast cancer risk. These findings align with prior research by Romieu et al., which similarly reported no significant association between reproductive factors and breast cancer among South African women [20].

Among premenopausal women, we observed a non-significant positive trend between increasing age and breast cancer risk, supporting the hypothesis that cumulative genetic mutations and prolonged exposure to endogenous hormones contribute to elevated risk with advancing age [21, 22].However, the lack of statistical significance may reflect limitations in statistical power due to the sample size.

Contrary to conventional evidence suggesting a protective role of parity, our findings did not show a significant association between parity and breast cancer risk. A recent meta-analysis indicated that high parity reduces the incidence of receptor-positive breast cancers by approximately 11%, while exerting no significant effect on receptor-negative subtypes [23]. That same analysis reported that delayed age at first birth was associated with a 27% higher risk of receptor-positive breast cancer. These subtype-specific differences underscore the molecular heterogeneity of breast cancer and caution against applying risk factors uniformly. The divergent biological pathways implicated in hormone receptor–positive and –negative tumors warrant separate evaluation of hormonal and reproductive influences.

Furthermore, previous studies have shown that exogenous hormone exposure is more strongly associated with ductal and lobular carcinomas in postmenopausal women than in premenopausal counterparts [24]. illustrating the complex interplay between menopausal status and breast cancer histology. Menopause itself serves as a significant biological modifier of hormonal effects on breast tissue [25]. In our study, reproductive factors did not show differential effects when stratified by menopausal status, although this may be partially attributed to limitations in accurately classifying menopausal state using self-reported data on hysterectomy, oophorectomy, and age.

Breastfeeding exhibited a non-significant inverse association with breast cancer risk (relative risk: 0.78), consistent with prior evidence suggesting that lactation may reduce cumulative estrogen exposure and induce terminal differentiation of breast epithelial cells [26]. Despite the lack of statistical significance, this observed trend warrants further investigation into larger cohorts.

Importantly, the absence of significance in some subgroup analyses should not obscure their clinical value. Stratified models can reveal nuanced patterns and trends potentially masked in aggregate analyses, offering critical insights into risk stratification. Age remains a robust and reproducible predictor of breast cancer risk and should continue to inform screening guidelines.

The strengths of this study lie in its stratified analytic approach and its focus on dissecting the contributions of reproductive variables across subgroups. Nonetheless, several limitations should be acknowledged: reliance on proxy variables for clinical outcomes (e.g., self-reported family history or previous breast surgery), small subgroup sample sizes, and potential recall bias in reporting reproductive histories.

5. Conclusion

The present analysis reveals a predominantly moderate parity distribution among the study population, with the highest frequency observed at four pregnancies. This pattern suggests a central tendency toward moderate reproductive histories, while both nulliparity and high multiparity were relatively uncommon. The skewed distribution underscores potential demographic, sociocultural, and health service influences on reproductive outcomes. These findings highlight the need for targeted reproductive health interventions, particularly to address the reproductive needs of women at both extremes of the parity spectrum, including those at risk of high-parity-related complications and those experiencing infertility or delayed childbearing.

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