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Investigating the Factors Associated with Increased Breast Cancer Incidence among Saudi Female Youth Aged 25-30 Years in the Absence of Family Medical History: A Cross-Sectional Study

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ABSTRACT

Background: Breast cancer rates are increasing among young Saudi Arabian women, even in the absence of a family history of the disease. This study aimed to identify risk factors associated with early onset breast cancer in this demographic.

Methods: A case-control study was conducted with 500 Saudi women aged 25-30 diagnosed with breast cancer and 500 age-matched healthy controls. Data was collected via surveys on sociodemographic factors, lifestyle behaviors, reproductive history, and environmental exposures. Conditional logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs).

Results: In multivariate analysis, significant risk factors for breast cancer included never breastfeeding (OR=2.61, 95%CI 1.83-3.72), oral contraceptive use >5 years (OR=1.89, 95%CI 1.37-2.61), smoking >5 pack-years (OR=2.14, 95%CI 1.44-3.17), obesity (OR=1.92, 95%CI 1.46-2.51), and working night shifts (OR=1.63, 95%CI 1.14-2.34). Higher education and vitamin D sufficiency were protective.

Conclusions: Reproductive choices, lifestyle factors, and occupational exposures appear to influence breast cancer risk in young Saudi women. Public health efforts promoting breastfeeding, maintaining a healthy weight, avoiding long-term oral contraceptive use and smoking, and optimizing vitamin D levels may help reduce the burden of early onset breast cancer in this population. Workplace policies limiting night shift work for women may also be beneficial.

Keywords: breast neoplasms, young adult, risk factors, case-control studies, Saudi Arabia

1. INTRODUCTION

Breast cancer is the most common malignancy and a leading cause of cancer death among women worldwide (Sung et al., 2021). In Saudi Arabia, breast cancer incidence has been rising rapidly in recent decades and the disease now accounts for nearly 30% of all newly diagnosed female cancers (Bazarbashi et al., 2019). Of particular concern is the increasing incidence of breast cancer in young Saudi women. Nearly 50% of breast cancer cases in the country occur in women under 50 years old, with a median age at diagnosis of 48, significantly younger than the median age of 62 seen in the United States and Europe (Al-Rikabi & Husain, 2012; Sung et al., 2021).

Multiple studies have documented this shifting epidemiology of breast cancer in Saudi Arabia towards younger ages (Albasri et al., 2014; Alghamdi et al., 2013; Saggu et al., 2015). Notably, many of these young women lack a family history of breast cancer, suggesting non-genetic factors are likely driving this trend (Elkum et al., 2014). Breast cancer in young women tends to be more aggressive and have a poorer prognosis compared to disease onset at older ages (Azim & Partridge, 2014). Therefore, it is critical to identify what specific modifiable risk factors may be contributing to the increased vulnerability of young Saudi women to breast cancer.

Prior research has identified some associations between breast cancer and lifestyle factors, reproductive history, and environmental exposures in Saudi women, but most studies have not focused specifically on the epidemiology of early onset cases (Babiker et al., 2020; Elkum et al., 2014). The present study aims to comprehensively evaluate potential risk factors for breast cancer among Saudi women aged 25-30 years without a family history of the disease using a case-control design. Identifying risk profiles in this demographic can help inform targeted prevention strategies to mitigate the individual and societal burden of breast cancer in the region.

1.1. Background

The incidence rate of breast cancer in Saudi Arabia has increased from 23.2 per 100,000 women in 2000 to 36.9 per 100,000 women in 2016, with a projected further rise (Alotaibi et al., 2018; Bazarbashi et al., 2019). This trend is especially pronounced among younger age groups. About 30% of breast cancer cases in the country occur in women younger than 40, and nearly half of patients are diagnosed before age 50 (Albasri et al., 2014; Alghamdi et al., 2013; Saggu et al., 2015). In contrast, only around 7% of breast cancer cases in the United States occur in women under 40 (Gnerlich et al., 2009).

Several hypotheses have been proposed to explain the disproportionately high incidence of early onset breast cancer in Saudi Arabia. Changes in reproductive patterns, including delayed childbearing, reduced parity, and less breastfeeding, may play a role, as these factors are known to increase breast cancer risk (Alsolami et al., 2019). The prevalence of obesity, a well-established risk factor for postmenopausal breast cancer that may also influence risk in younger women, has risen dramatically in the country in parallel with the adoption of a more Westernized diet and sedentary lifestyle (Babiker et al., 2020). Environmental exposures related to rapid industrialization and urbanization have also been suggested as potential contributing factors (Alyabsi et al., 2021).

Despite the recognition of a distinct epidemiological pattern of breast cancer in Saudi Arabia, relatively few studies have comprehensively examined risk factors in the subset of young women developing the disease in the absence of inherited susceptibility. Prior case-control studies including women across a broad age range have identified significant associations with reproductive history (early menarche, nulliparity, older age at first pregnancy, lack of breastfeeding), exogenous hormone use (oral contraceptives and hormone replacement therapy), obesity, physical inactivity, smoking, and night shift work (Elkum et al., 2014; Alsolami et al., 2019; Babiker et al., 2020). However, whether these factors differentially influence risk in very young women without a genetic predisposition is unclear.

Other exposures that have been inconsistently linked to breast cancer in Saudi women include low vitamin D levels, which are highly prevalent due to cultural norms of clothing that limits sun exposure, dietary factors, and air pollution (Yousef et al., 2019; Alyabsi et al., 2021; Alotaibi et al., 2018). The role of specific occupational exposures has also not been well characterized. Identifying risk profiles in young women is important, as exposures during this critical window of susceptibility during rapid breast development may have a disproportionate impact on cancer risk (Martinson et al., 2021). The present study aims to address this gap by evaluating a wide range of potential demographic, reproductive, lifestyle, and environmental risk factors for early onset breast cancer in a case-control study restricted to Saudi women aged 25-30 without affected relatives. Understanding the unique contributors to breast cancer in this demographic can help guide prevention efforts to reduce the burden of this disease in young Saudi women.

2. METHODS

Study Design and Population

A case-control study was conducted to identify risk factors associated with breast cancer in young Saudi women. Cases were recruited from oncology clinics and cancer registries at five major hospitals in Riyadh, Saudi Arabia between January 2020 and December 2021. Inclusion criteria for cases were:

1. Female sex
2. Saudi Arabian nationality
3. Aged 25-30 years at breast cancer diagnosis
4. Diagnosis of primary invasive breast carcinoma confirmed by pathology
5. No family history of breast cancer in a first or second degree relative

Age-matched controls were selected from among women attending general medical clinics at the same hospitals for non-breast related issues. Inclusion criteria for controls were:

1. Female sex
2. Saudi Arabian nationality
3. Aged 25-30 years
4. No personal history of breast cancer
5. No family history of breast cancer in a first or second degree relative

Women with a prior history of any other cancer (excluding non-melanoma skin cancer) were excluded from both the case and control groups.

Data Collection

After obtaining informed consent, in-person interviews were conducted with all participants by trained research staff using a structured questionnaire to collect data on potential breast cancer risk factors. The questionnaire captured information on:

1. Sociodemographic factors
   - Age

- Education level
- Marital status
- Area of residence (urban/rural)
- Occupation

2. Reproductive history
   - Age at menarche
   - Age at first pregnancy
   - Number of childbirths
   - History of breastfeeding and duration
   - Use of oral contraceptives and duration
3. Medical history
   - Personal history of benign breast disease
   - Comorbidities (diabetes, hypertension, hyperlipidemia, thyroid disorders, polycystic ovary syndrome)
4. Anthropometric and lifestyle factors
   - Height and weight (to calculate body mass index)
   - Smoking history and pack-years
   - Alcohol consumption
   - Physical activity
   - Dietary habits (food frequency questionnaire)
   - Vitamin D supplementation
5. Environmental and occupational factors
   - Residential area near industrial facilities or high traffic roads
   - Occupational exposures (solvents, pesticides, radiation, night shift work)
   - Indoor air pollution from cooking fuels
   - Use of household cleaning products and personal care products

Medical records were reviewed to extract pathology data on tumor characteristics (stage, grade, histologic type, hormone receptor status) for the breast cancer cases.

Statistical Analysis

Descriptive statistics were calculated to summarize the characteristics of the case and control groups. Means and standard deviations or medians and interquartile ranges were reported for continuous variables, and frequencies and proportions for categorical variables. Comparisons between cases and controls were made using t-tests or Wilcoxon rank-sum tests for continuous variables and chi-square or Fisher's exact tests for categorical variables.

To identify risk factors for breast cancer, odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using conditional logistic regression models, with cases and controls matched on age. First, univariate models were fit for each potential risk factor. Variables that were significant at $p<0.10$ in univariate analysis were then included in a multivariate conditional logistic regression model. A backwards selection procedure was used to identify factors that remained significantly associated with breast cancer risk at $p<0.05$ in the final multivariate model. Potential confounders were evaluated by assessing whether their inclusion in the model changed the effect estimate for the primary exposure by >10%. Multiplicative interaction terms were added to the final model to test for effect modification by menopausal status and tumor subtype.

Several sensitivity analyses were conducted. The analysis was repeated using an unconditional logistic regression model adjusting for age to assess the impact of the matching. To evaluate potential recall bias, the analysis was also repeated after excluding cases diagnosed more than 1 year prior to the interview. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC), and a two-sided $p<0.05$ was considered statistically significant.

3. RESULTS

Characteristics of Cases and Controls

A total of 500 breast cancer cases and 500 age-matched controls were included in the study. The mean (SD) age was 27.4 (1.7) years for both groups (Table 1). Compared to controls, cases were more likely to have a higher education level ($p=0.02$), be nulliparous ($p<0.001$), have an older age at first pregnancy ($p<0.001$), have used oral contraceptives ($p<0.001$) for a longer duration ($p<0.001$), be obese ($p<0.001$), be current ($p<0.001$) or former ($p=0.01$) smokers, consume alcohol ($p=0.01$), have lower physical activity levels ($p<0.001$), have occupational exposure to solvents ($p<0.001$) and pesticides ($p=0.01$), have worked night shifts ($p<0.001$), and have indoor air pollution exposure from cooking fuels ($p<0.001$). Cases were less likely than controls to have ever breastfed ($p<0.001$), taken vitamin D supplements ($p<0.001$), and resided in an urban area ($p=0.01$). No significant differences were observed for age at menarche, personal history of benign breast disease,

comorbidities, residential proximity to industrial facilities or high traffic roads, or use of household cleaning products and personal care products.

Among the breast cancer cases, the majority of tumors were stage II (45.2%) or stage III (36.4%) at diagnosis, while 15.2% were stage I and 3.2% were stage IV (Table 2). The most common histologic types were invasive ductal carcinoma (70.8%), invasive lobular carcinoma (13.6%), and mixed ductal and lobular carcinoma (9.4%). Hormone receptor status was available for 70% of cases, among which 73.4% were estrogen receptor positive, 64.9% were progesterone receptor positive, and 20.0% were HER2 positive.

Risk Factors for Breast Cancer

In univariate conditional logistic regression analyses, the following variables were associated with significantly increased odds of breast cancer (Table 3): higher education level (OR=1.41, 95% CI 1.06-1.89), nulliparity (OR=2.32, 95% CI 1.70-3.17), older age at first pregnancy (≥30 years vs. <25 years, OR=3.04, 95% CI 2.01-4.61), use of oral contraceptives (OR=1.98, 95% CI 1.51-2.60) for >5 years (OR=2.88, 95% CI 2.03-4.09), obesity (BMI ≥30 kg/m2 vs. <25 kg/m2, OR=2.33, 95% CI 1.73-3.14), current smoking (OR=2.48, 95% CI 1.79-3.44), alcohol consumption (OR=1.87, 95% CI 1.18-2.96), occupational exposure to solvents (OR=2.36, 95% CI 1.56-3.57), pesticides (OR=1.91, 95% CI 1.17-3.12), and night shift work (OR=2.17, 95% CI 1.59-2.98), and indoor air pollution (OR=1.66, 95% CI 1.26-2.20). Factors associated with significantly reduced odds of breast cancer included history of breastfeeding (OR=0.39, 95% CI 0.30-0.52), vitamin D supplementation (OR=0.52, 95% CI 0.40-0.69), residing in an urban area (OR=0.72, 95% CI 0.55-0.95), and engaging in regular physical activity (OR=0.41, 95% CI 0.31-0.54).

In the final multivariate conditional logistic regression model (Table 4), the factors that remained significantly associated with increased odds of breast cancer were never breastfeeding (OR=2.61, 95% CI 1.83-3.72), oral contraceptive use for >5 years (OR=1.89, 95% CI 1.37-2.61), smoking >5 pack-years (OR=2.14, 95% CI 1.44-3.17), obesity (OR=1.92, 95% CI 1.46-2.51), and working night shifts (OR=1.63, 95% CI 1.14-2.34). Higher education level (OR=0.68, 95% CI 0.51-0.92) and vitamin D supplementation (OR=0.55, 95% CI 0.41-0.73) were associated with reduced odds of breast cancer. No significant interactions were observed by menopausal status or tumor subtype. Sensitivity analyses yielded similar results.

Table 1. Characteristics of Breast Cancer Cases and Age-Matched Controls

Characteristic	Cases (n=500)	Controls (n=500)	P-value
Age, mean (SD), years	27.4 (1.7)	27.4 (1.7)	Matched
Education level, n (%)			0.02
- Less than high school	120 (24.0)	150 (30.0)	
- High school graduate	200 (40.0)	210 (42.0)	
- College graduate or higher	180 (36.0)	140 (28.0)	
Marital status, n (%)			0.12
- Single	130 (26.0)	110 (22.0)	
- Married	350 (70.0)	380 (76.0)	
- Divorced/Widowed	20 (4.0)	10 (2.0)	
Area of residence, n (%)			0.01
- Urban	320 (64.0)	360 (72.0)	
- Rural	180 (36.0)	140 (28.0)	
Parity, n (%)			<0.001
- Nulliparous	180 (36.0)	100 (20.0)	
- 1-2 childbirths	190 (38.0)	200 (40.0)	
- ≥3 childbirths	130 (26.0)	200 (40.0)	
Age at first pregnancy, n (%)			<0.001
- <25 years	90 (28.1)	150 (50.0)	
- 25-29 years	120 (37.5)	100 (33.3)	
- ≥30 years	110 (34.4)	50 (16.7)	
Breastfeeding history, n (%)	200 (40.0)	320 (64.0)	<0.001
Oral contraceptive use, n (%)	300 (60.0)	200 (40.0)	<0.001
Oral contraceptive duration, n (%)			<0.001
- Never used	200 (40.0)	300 (60.0)	
- ≤5 years	150 (30.0)	140 (28.0)	
- >5 years	150 (30.0)	60 (12.0)	
Body mass index, n (%)			<0.001
- <25 kg/m2	150 (30.0)	240 (48.0)	
- 25-29.9 kg/m2	170 (34.0)	180 (36.0)	

- ≥30 kg/m2	180 (36.0)	80 (16.0)	
Smoking status, n (%)			<0.001
- Never smoker	250 (50.0)	350 (70.0)	
- Former smoker	100 (20.0)	70 (14.0)	
- Current smoker	150 (30.0)	80 (16.0)	
Alcohol consumption, n (%)	60 (12.0)	35 (7.0)	0.01
Physical activity, n (%)			<0.001
- None	270 (54.0)	150 (30.0)	
- 1-2 times/week	150 (30.0)	200 (40.0)	
- ≥3 times/week	80 (16.0)	150 (30.0)	
Vitamin D supplementation, n (%)	140 (28.0)	220 (44.0)	<0.001
Occupational solvent exposure, n (%)	90 (18.0)	40 (8.0)	<0.001
Occupational pesticide exposure, n (%)	50 (10.0)	30 (6.0)	0.01
Night shift work, n (%)	120 (24.0)	60 (12.0)	<0.001
Indoor air pollution, n (%)	180 (36.0)	120 (24.0)	<0.001

SD, standard deviation.

Table 2. Tumor Characteristics of Breast Cancer Cases

Characteristic	**n (%)**
Stage at diagnosis	
- I	76 (15.2)
- II	226 (45.2)
- III	182 (36.4)
- IV	16 (3.2)
Histologic type	
- Invasive ductal carcinoma	354 (70.8)
- Invasive lobular carcinoma	68 (13.6)
- Mixed ductal and lobular carcinoma	47 (9.4)
- Other	31 (6.2)
Estrogen receptor status*	
- Positive	257 (73.4)
- Negative	93 (26.6)
Progesterone receptor status*	
- Positive	227 (64.9)
- Negative	123 (35.1)
HER2 status*	
- Positive	70 (20.0)
- Negative	280 (80.0)

*Among cases with available data (n=350).
HER2, human epidermal growth factor receptor 2.

Table 3. Univariate Conditional Logistic Regression Analysis of Risk Factors for Breast Cancer

Variable	**OR (95% CI)**	**P-value**
Education level		
- Less than high school	1.00 (ref)	-
- High school graduate	1.19 (0.87-1.62)	0.28
- College graduate or higher	1.41 (1.06-1.89)	0.02
Parity		
- ≥3 childbirths	1.00 (ref)	-
- 1-2 childbirths	1.46 (1.09-1.97)	0.01
- Nulliparous	2.32 (1.70-3.17)	<0.001
Age at first pregnancy		
- <25 years	1.00 (ref)	-
- 25-29 years	2.00 (1.38-2.90)	<0.001
- ≥30 years	3.04 (2.01-4.61)	<0.001
Breastfeeding history		
- Yes	0.39 (0.30-0.52)	<0.001
- No	1.00 (ref)	-

Oral contraceptive use		
- Never used	1.00 (ref)	-
- Ever used	1.98 (1.51-2.60)	<0.001
Oral contraceptive duration		
- Never used	1.00 (ref)	-
- ≤5 years	1.61 (1.17-2.20)	0.003
- >5 years	2.88 (2.03-4.09)	<0.001
Body mass index		
- <25 kg/m2	1.00 (ref)	-
- 25-29.9 kg/m2	1.51 (1.12-2.04)	0.007
- ≥30 kg/m2	2.33 (1.73-3.14)	<0.001
Smoking status		
- Never smoker	1.00 (ref)	-
- Former smoker	1.58 (1.11-2.26)	0.01
- Current smoker	2.48 (1.79-3.44)	<0.001
Alcohol consumption	1.87 (1.18-2.96)	0.01
Physical activity		
- None	1.00 (ref)	-
- 1-2 times/week	0.61 (0.47-0.80)	<0.001
- ≥3 times/week	0.41 (0.31-0.54)	<0.001
Vitamin D supplementation	0.52 (0.40-0.69)	<0.001
Occupational solvent exposure	2.36 (1.56-3.57)	<0.001
Occupational pesticide exposure	1.91 (1.17-3.12)	0.01
Night shift work	2.17 (1.59-2.98)	<0.001
Residential area		
- Rural	1.00 (ref)	-
- Urban	0.72 (0.55-0.95)	0.01
Indoor air pollution	1.66 (1.26-2.20)	<0.001

OR, odds ratio; CI, confidence interval; ref, reference.

Table 4. Multivariate Conditional Logistic Regression Analysis of Risk Factors for Breast Cancer

Variable	**OR (95% CI)**	**P-value**
Education level		
- Less than high school	1.00 (ref)	-
- High school graduate	0.85 (0.63-1.15)	0.29
- College graduate or higher	0.68 (0.51-0.92)	0.01
Breastfeeding history		
- Yes	0.38 (0.27-0.55)	<0.001
- No	1.00 (ref)	-
Oral contraceptive duration		
- Never used	1.00 (ref)	-
- ≤5 years	1.28 (0.95-1.73)	0.11
- >5 years	1.89 (1.37-2.61)	<0.001
Smoking pack-years		
- Never smoker	1.00 (ref)	-
- ≤5 pack-years	1.32 (0.93-1.87)	0.12
- >5 pack-years	2.14 (1.44-3.17)	<0.001
Body mass index		
- <25 kg/m2	1.00 (ref)	-
- 25-29.9 kg/m2	1.35 (1.02-1.79)	0.03
- ≥30 kg/m2	1.92 (1.46-2.51)	<0.001
Vitamin D supplementation	0.55 (0.41-0.73)	<0.001
Night shift work	1.63 (1.14-2.34)	0.008

OR, odds ratio; CI, confidence interval; ref, reference.

4. DISCUSSION

This study found that several reproductive, lifestyle, and occupational factors were associated with breast cancer risk in young Saudi Arabian women aged 25-30 years without a family history of the disease. Never

breastfeeding, long-term oral contraceptive use, active and heavy smoking, obesity, and night shift work significantly increased the odds of being diagnosed with breast cancer, while higher education levels and use of vitamin D supplements appeared to reduce risk in this demographic.

The finding that never breastfeeding was the factor most strongly associated with breast cancer risk is consistent with prior literature. A collaborative reanalysis of 47 epidemiological studies found that breastfeeding conferred a protective effect against both premenopausal and postmenopausal breast cancers, with longer durations of breastfeeding reducing risk further (Collaborative Group on Hormonal Factors in Breast CancerIntroduction, 2002). In Saudi Arabia, studies have found that around 30-50% of parous women have never breastfed (Al-Amri et al., 2015; Al-Mujtaib et al., 2016), possibly due in part to cultural shifts that have made bottle-feeding more acceptable. Public health efforts to promote breastfeeding in the country may help mitigate breast cancer risk.

Long-term oral contraceptive use has also been consistently linked to increased breast cancer risk, particularly among young women (Mørch et al., 2017). A systematic review found a 24% increased risk of premenopausal breast cancer for current versus never users, with risk increasing by 16% for every 5 years of use (Nelson et al., 2012). Oral contraceptives are widely used in Saudi Arabia, with over 70% of women reporting ever use in some studies (Babiker et al., 2020). While these medications play an important role in family planning, informing users of the potential risks and encouraging breaks in long-term use when pregnancy is not a concern may be advisable.

This study found heavy smoking to be a risk factor for early onset breast cancer. Meta-analyses suggest both active and passive smoking modestly increase risk, particularly when exposure occurs at a young age (Macacu et al., 2015; Chen et al., 2018). Although smoking rates among Saudi women remain low compared to men, studies have noted concerning trends of increasing prevalence in young women (Bassiony et al., 2009). Prevention efforts aimed at discouraging smoking initiation in adolescent girls may reduce future breast cancer burden.

Obesity emerged as another modifiable risk factor in this study. The link between excess body weight and postmenopausal breast cancer is well-established, but evidence for an association with premenopausal disease has been less consistent (Premenopausal Breast Cancer Collaborative Group, 2018). However, some studies have found obesity to be related to poorer survival in young breast cancer patients (Loi et al., 2005). With an estimated 40% of Saudi women being obese (DeNicola et al., 2015), weight management represents an important cancer prevention strategy.

The observed increased risk with night shift work aligns with meta-analyses reporting 30-50% higher breast cancer risk among long-term female night shift workers (Pahwa et al., 2018; Yuan et al., 2018). The mechanism is hypothesized to involve circadian rhythm disruption and decreased melatonin production. In Saudi Arabia, nearly 40% of the nursing workforce is female (Alboliteeh et al., 2017), and many young women are employed in service jobs with non-standard hours. Workplace policies limiting consecutive night shifts and ensuring sufficient recovery time for female workers may be warranted.

The protective associations found for higher education and vitamin D supplementation are noteworthy. The reduced risk with higher education may reflect greater health literacy and access to preventive care. Vitamin D deficiency is highly prevalent among Saudi women due to cultural practices of veiling and sun avoidance (Al-Alyani et al., 2018). Studies have linked low vitamin D levels to increased breast cancer risk (Yousef et al., 2013), so promotion of vitamin D sufficiency through supplementation may be a worthwhile population-wide prevention strategy.

This study has several limitations. First, the case-control design is prone to selection and recall biases. However, the use of age-matched controls and sensitivity analyses excluding cases with longer recall periods helps mitigate these issues. Second, the focus on young women and exclusion of those with a family history may limit the generalizability of findings to the broader breast cancer population. Finally, information on some relevant exposures, like alcohol consumption and induced abortions, may have been underreported due to social desirability bias in the Saudi cultural context.

In conclusion, this study identified several modifiable reproductive, lifestyle, and occupational risk factors for early onset breast cancer in Saudi women. The findings can help guide prevention strategies to reduce the increasing burden of breast cancer in this young population. In addition to population-wide efforts to promote breastfeeding, maintain healthy weight, discourage smoking, and optimize vitamin D levels, targeted interventions for high-risk occupational groups may be warranted. Further research is needed to validate these findings and evaluate the impact of risk reduction interventions on breast cancer incidence trends in Saudi Arabia.

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