Genetic, Hormonal, and Cultural Determinants of Breast Cancer Risk Among Egyptian Women Under 50 Years

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Abstract

Background: Breast cancer is a leading cause of morbidity and mortality globally, with increasing incidence in women under 50 years, particularly in developing countries like Egypt. **Objective:** To investigate genetic, hormonal, and cultural determinants of breast cancer risk among Egyptian women under 50 years and to analyze their associations with socio-demographic, medical, reproductive, lifestyle, and psychosocial factors. **Methods:** A case-control study was conducted involving 103 breast cancer cases and 208 controls. Data were collected via expert-reviewed questionnaires and biochemical assessments of serum estradiol (E2) and oxytocin (OT) levels. Statistical analyses included chi-square tests, t-tests, and logistic regression to identify significant risk factors and predictors. **Results:** Majority of BC cases (64.1%) were aged 41–49 years, with a mean age of 40.56 ± 6.65. Illiteracy and being a housewife were significantly associated with higher BC risk. Medical history such as hypertension, diabetes, bone ache, and hormonal treatment showed strong links to BC, especially hormonal therapy (OR=19.46). Logistic regression revealed oral contraceptive use (OR=20.00), family history (OR=18.47), smoking (OR=14.87), physical inactivity, and CYP17 gene polymorphism as major predictors. Psychosocial factors such as emotional dissatisfaction and low sexual satisfaction were also significant. Age and CYP19 polymorphism were not significant predictors. **Conclusions:** Breast cancer risk among Egyptian women under 50 is multifactorial, influenced by genetic predisposition, hormonal exposure, lifestyle, and psychosocial factors. **Recommendations:** Implement targeted educational programs on modifiable risk factors, integrate comprehensive risk assessments and address psychosocial well-being in prevention strategies. **Keywords:** Breast cancer, risk factors, genetics, hormonal treatment, lifestyle, psychosocial, CYP17 polymorphism.

Introduction

Breast cancer (BC) remains a leading cause of morbidity and mortality worldwide and is the most frequently diagnosed cancer among women globally **(Sung et al., 2021).** It ranks as the second most common cancer next to lung cancer and is a critical public health concern due to its profound social and economic impact. While BC incidence generally increases with age, women under 50 years also represent a significant proportion of cases, especially in developing regions like Egypt where the median age of diagnosis is notably younger compared to Western populations **(Siegel et al., 2018).** This younger age at onset may be influenced by a combination of genetic predispositions, hormonal profiles, and cultural factors unique to the Egyptian population.

Genetic factors play a crucial role in BC susceptibility. Besides the well-documented high-penetrance genes such as BRCA1 and BRCA2 mutations, low-penetrance genetic variations also contribute substantively to BC risk through altering estrogen biosynthesis and metabolism **(García-Sancha et al., 2025).** Polymorphisms in genes like CYP17 and CYP19, encoding enzymes involved in steroid hormone pathways, can influence endogenous estrogen levels, which is a critical factor in carcinogenesis **(Alwan & Afzaljavan, 2022).** Elevated lifetime exposure to estrogens, particularly estradiol (E2), is strongly associated with increased risk, especially in hormone receptor-positive BC subtypes **(Richman & Dowsett, 2019).**

Hormonal factors beyond endogenous estrogen also affect BC risk. The use of exogenous hormones, such as oral contraceptive pills (OCPs) and hormone replacement therapy, has been linked to elevated BC risk, especially when initiated at younger ages and prolonged use **(Satish et al., 2023).** Moreover, life stages such as early menarche, delayed childbearing, nulliparity, and late menopause extend estrogen exposure duration, contributing to earlier onset and higher incidence of BC **(Mishra et al., 2021).**

Cultural determinants, particularly in the Egyptian context, also affect BC risk profiles. Cultural practices often lead to delayed onset of regular sexual activity due to premarital chastity norms, which may reduce oxytocin (OT) levels; OT is implicated in breast tissue regulation and may exert protective effects against carcinogenesis **(Elhawary et al., 2025).** Furthermore,

reproductive behaviors such as breastfeeding duration, marriage patterns, and parity influenced by cultural norms can modify BC risk **(El Sharif & Khatib, 2021).**

Environmental and lifestyle factors also intersect with genetic and hormonal influences to modulate BC risk in young women. Factors such as physical inactivity, smoking, diet rich in saturated fats, and environmental pollutant exposure have been associated with increased BC risk **(Vegunta et al., 2020).**

Given this multifactorial etiology involving genetic polymorphisms, hormone levels, and culturally determined behaviors, there is a pressing need to understand their combined impact on BC risk among Egyptian women under 50. This understanding is crucial to develop targeted prevention strategies, improve early detection, and tailor interventions appropriate to this demographic. Investigating these determinants offers potential to inform clinical risk prediction models and public health initiatives aimed at reducing BC burden in Egypt and similar populations.

Aim of the Study:

To study genetic, hormonal and cultural determinants of breast cancer risk among Egyptian women under 50 years."

Research Questions

1. What is the association between CYP17 and CYP19 genetic polymorphisms and the risk of breast cancer among Egyptian women under 50 years?
2. How are serum estradiol (E2) and oxytocin (OT) levels related to the age of breast cancer diagnosis in Egyptian women under 50 years?
3. Does the age at initiation of regular sexual activity, as a culturally determined factor, influence the risk of breast cancer in young Egyptian women?

Subjects and methods

Subjects

This study included women under 50 years of age diagnosed with breast cancer and age-matched controls without breast cancer. The subjects were recruited from the Oncology Departments of Alexandria University Hospital and affiliated medical centers. A total of 250 breast cancer cases and 250 controls were enrolled during the 18-month study period from January 2022 to June 2023. Controls were selected from women attending general outpatient clinics for conditions unrelated to cancer and were matched to cases by age (±2 years) and residential area. Women with a previous history of any malignancy or chronic debilitating illness were excluded.

Research Design

The present study employed a hospital-based matched case–control design to investigate genetic, hormonal, and cultural determinants associated with breast cancer in women under the age of 50.

Setting

The study was conducted in the Oncology Departments of Alexandria University Hospital and other affiliated healthcare centers providing cancer diagnostic and treatment services.

Tools of the Study

Data were collected using a structured, pretested questionnaire designed by the researchers and validated by oncology and epidemiology experts. It covered the following domains:

-Sociodemographic data: age, marital status, education, occupation, and residence.

-Familial history: breast cancer and other cancers among first- and second-degree relatives.

-Reproductive and hormonal factors: age at menarche, parity, age at first childbirth, breastfeeding, contraceptive use, hormone replacement therapy.

-Genetic factors: family pedigree analysis and BRCA1/BRCA2 testing where available.

-Behavioral and cultural factors: dietary practices, physical activity, smoking, alcohol consumption, and health-seeking behaviors.

-Medical history: comorbidities such as diabetes, hypertension, and prior benign breast disease.

Method

Obtaining Approval: Official permissions were secured from hospital administrations before data collection.

Ethical Considerations: The study protocol was approved by the Ethics Committee of Alexandria University. Written informed consent was obtained from all participants after explaining study objectives. Privacy and confidentiality were strictly maintained.

Preparation of Study Tools: The questionnaire underwent expert review and a pilot study with 20 participants to assess clarity and reliability. Adjustments were made accordingly.

Data Collection: Trained female interviewers administered the questionnaire during face-to-face interviews and reviewed medical records for clinical verification.

Statistical Analysis: Data were analyzed using SPSS version 25.0. Continuous variables were summarized as means ± SD, while categorical variables were presented as frequencies and percentages. Odds ratios (OR) with 95%

confidence intervals (CI) were calculated using conditional logistic regression to identify significant predictors of breast cancer. A p-value of <0.05 was considered statistically significant.

Table (1) presents the age distribution of breast cancer (BC) cases and controls. The majority of cases (64.1%) fall within the 41–49 age group, compared to 45.2% of controls, indicating a higher risk in older premenopausal women. The 20–30 age group shows a lower proportion of cases (7.7%) relative to controls (12.0%). The chi-square test demonstrates a statistically significant association between age group and BC occurrence (χ^2=9.837, p=0.009). The mean age of cases (40.56 ± 6.65 years) is significantly higher than controls (38.39 ± 7.18 years; t=2.574, p=0.011), supporting age as a potential risk factor for BC in this cohort.

Table (2) illustrates the distribution of breast cancer (BC) cases and controls across key socio-demographic factors. Residence showed no significant association with BC, as urban versus rural location had an OR of 1.336 and a p-value of 0.247. Education level, however, demonstrated a strong effect: illiterate participants had nearly four times higher odds of BC compared to university-educated individuals (OR = 3.990, p < 0.001). Occupation was also highly significant, with housewives showing over fourfold increased odds and manual workers exhibiting extremely elevated risk relative to professionals, highlighting the influence of social determinants on BC prevalence. These findings underscore education and occupation as critical risk factors.

Table (3) highlights a significant association between medical history factors and breast cancer (BC) occurrence. Cases had notably higher proportions of hypertension (33.0% vs. 11.5%), diabetes mellitus (33.0% vs. 13.9%), bone ache (16.5% vs. 1.4%), and prior hormonal treatment (54.4% vs. 5.8%) compared to controls. All factors reached statistical significance (p < 0.001), with odds ratios indicating substantial increased risks: hormonal treatment (OR = 19.46) and bone ache (OR = 13.51) were the strongest predictors, followed by hypertension (OR = 3.78) and diabetes (OR = 3.04). These findings suggest that both metabolic conditions and exogenous hormone exposure markedly elevate BC risk, highlighting the importance of comprehensive medical history assessment in risk stratification.

Table 4 presents the distribution of breast cancer (BC) cases and controls according to reproductive history. No significant differences were observed for age at menarche or age at marriage, suggesting these factors may not strongly influence BC risk in this cohort. Marital status was significantly associated with BC, with a higher proportion of cases being married (96.1% vs. 81.7%, p=0.002), indicating a potential protective or risk-modifying effect of marital factors. Menopausal status showed a strong association with BC (40.7% vs. 13.9%, p<0.001), suggesting increased risk post-menopause. Breastfeeding duration showed no significant difference, indicating limited impact on BC risk in this population

Table 5 presents a logistic regression analysis identifying significant predictors of the outcome. The results highlight that use of oral contraceptive pills (OR = 20.002), positive family history (OR = 18.472), and smoking (OR = 14.873) are the strongest risk factors, all with highly significant p-values (<0.001). Physical inactivity and CYP17 polymorphism also show substantial associations (OR = 10.197 and 7.115, respectively). Moderate but significant contributions come from saturated fat intake, emotional dissatisfaction, and low sex satisfaction (ORs = 6.152, 2.361, 1.631). In contrast, CYP19 polymorphism and age were not statistically significant, indicating minimal impact in this model. These findings underscore lifestyle, genetic, and hormonal influences on risk.

Table 6 highlights multiple significant predictors of breast cancer in women under 50, spanning hormonal, genetic, lifestyle, dietary, and psychosocial domains. Hormonal exposure via oral contraceptives and genetic factors, including family history and CYP17 polymorphisms, underscore both endogenous and inherited risks. Modifiable lifestyle factors such as smoking, physical inactivity, and high saturated fat intake further emphasize the role of behavior in disease susceptibility. Interestingly, psychosocial elements like emotional dissatisfaction and low sexual satisfaction also emerge as significant, suggesting that psychological well-being may influence cancer risk. Overall, this multifactorial profile supports a holistic approach to breast cancer prevention and risk assessment.

Table (1): Distribution of (BC) cases and controls according to Age

Age Group	Cases (n=103)	Controls (n=208)	χ^2	p-value	OR	95% CI
20–30	8 (7.7%)	25 (12.0%)	9.837	0.009*	Ref	–
31–40	29 (28.2%)	89 (42.8%)			1.018	0.414–2.504
41–49	66 (64.1%)	94 (45.2%)			2.194	0.932–5.165
Mean ± SD	40.56 ± 6.65	38.39 ± 7.18	t=2.574	0.011*	–	–

Table (2): Distribution of (BC) cases and controls according to Socio-demographic Factors

Factor	Cases (n=103)	Controls (n=208)	χ^2	p-value	OR	95% CI
Residence						
Urban	40 (38.8%)	67 (32.2%)	–	0.247	1.336	0.817–2.184
Rural	63 (61.2%)	141 (67.8%)	–	Ref	–	–
Education						
Illiterate	76 (73.8%)	80 (38.5%)	43.553	<0.001*	3.990	1.432–11.116
University	5 (4.9%)	21 (10.1%)	Ref	–	–	–
Occupation						
Professional	3 (2.9%)	63 (30.3%)	39.589	<0.001*	Ref	–
Housewife	90 (87.4%)	136 (65.5%)			13.897	4.234–45.610
Manual	3 (2.9%)	3 (1.4%)			21.000	2.913–151.408

Table (3): Distribution of (BC) cases and controls according to Medical History

Factor	Cases (n=103)	Controls (n=208)	χ^2	p-value	OR	95% CI
Hypertension	34 (33.0%)	24 (11.5%)	20.933	<0.001*	3.778	2.091–6.824
Diabetes mellitus	34 (33.0%)	29 (13.9%)	15.504	<0.001*	3.041	1.724–5.367
Bone ache	17 (16.5%)	3 (1.4%)	25.974	<0.001*	13.508	3.859–47.286
Hormonal treatment	56 (54.4%)	12 (5.8%)	95.239	<0.001*	19.461	9.664–39.191

Table (4): Distribution of (BC) cases and controls according to Reproductive History

Factor	Cases (n=103)	Controls (n=208)	χ^2 / t	p-value	OR	95% CI
Age at menarche (Mean ± SD)	12.97 ± 1.14	13.06 ± 1.00	t=0.730	0.466	1.042	0.728–1.150
Age at marriage (Mean ± SD)	20.48 ± 4.19	19.82 ± 3.85	t=1.378	0.169	–	–
Marital status (Married)	96.1%	81.7%	χ^2=14.564	0.002*	0.329	0.154–0.702
Menopause (Yes)	40.7%	13.9%	χ^2=58.079	<0.001*	4.249	0.450–1.061
Breastfeeding (months, Mean ± SD)	47.91 ± 32.45	52.45 ± 55.64	t=1.378	0.169	0.998	0.992–1.004

Table (5): Logistic Regression Analysis of Risk Factors

Predictor	OR	95% CI	p-value
Oral contraceptive pills (OCPs)	20.002	–	<0.001
Positive family history	18.472	–	<0.001
Smoking	14.873	–	<0.001
Physical inactivity	10.197	–	<0.01
CYP17 polymorphism (A1/A2 vs ND)	7.115	–	<0.05
Saturated fats	6.152	–	<0.05
Emotional dissatisfaction	2.361	–	<0.05
Low sex satisfaction	1.631	–	<0.05
CYP19 polymorphism	1.168	–	NS
Age	1.041	–	NS

Table (6): Significant Predictors of Breast Cancer (<50 years)

Predictor	Category / Nature	Significance
Hormonal treatment (OCPs)	Hormonal / Reproductive	Significant
Family history of BC	Genetic / Familial	Significant
Smoking habit	Lifestyle / Behavioral	Significant
Physical inactivity	Lifestyle / Behavioral	Significant
CYP17 gene polymorphism	Genetic / Molecular	Significant
Saturated fats intake	Dietary / Nutritional	Significant
Emotional dissatisfaction	Psychosocial / Cultural	Significant
Low sex satisfaction	Psychos	

Discussion

The results presented herein offer a comprehensive analysis of breast cancer (BC) risk factors among women under 50 years of age. The findings underscore the multifactorial nature of BC, encompassing age, socio-demographic factors, medical history, reproductive history, and lifestyle behaviors. This discussion contextualizes these results within the broader body of recent literature, highlighting areas of concordance and divergence.

The study's observation that the majority of BC cases (64.1%) fall within the 41–49 age group, with a mean age of 40.56 ± 6.65 years, aligns with global trends indicating

an increased incidence of BC in older premenopausal women. A study by **Kiss et al. (2023)** reported a significant increase in BC incidence among young females, with age-specific rates rising by 30.02% between 2011 and 2019. This suggests that while BC incidence is rising in younger populations, the risk remains notably higher in the 40–49 age group. The statistically significant association between age and BC occurrence in this study (χ^2=9.837, p=0.009) further corroborates these findings.

The study identifies education level and occupation as significant socio-demographic risk factors. Illiterate participants had nearly four times higher odds of BC compared to university-educated individuals, and housewives exhibited over fourfold increased odds relative to professionals. These findings are consistent with **Dong & Qin (2020)**, who found that higher education levels were associated with increased BC risk, potentially due to factors like alcohol use, age at menopause, and hormone therapy. Similarly, **Sari et al. (2020)** reported that job category and occupational activity were associated with BC risk, with high risk observed in office workers and women with sedentary jobs.

Interestingly, residence (urban vs. rural) did not show a significant association with BC in this study. This contrasts with some literature suggesting environmental and lifestyle differences between urban and rural populations may influence BC risk. However, the lack of significant association in this study may be attributed to the specific socio-economic context of the cohort.

The study highlights significant associations between BC and medical history factors such as hypertension, diabetes mellitus, bone ache, and prior hormonal treatment. Notably, hormonal treatment had an odds ratio (OR) of 19.46, and bone ache had an OR of 13.51, indicating substantial increased risks. These findings are supported by **Parrent et al. (2025)**, who reported that the risk of BC in type 2 diabetic women is increased by 10–20%, and **Connaughton & Dabagh, (2022)**, who found that hypertension, is independently associated with increased cancer risk. The strong association with hormonal treatment aligns with existing literature emphasizing the role of exogenous hormones in BC risk.

The study found no significant differences in age at menarche or age at marriage between BC cases

and controls, suggesting these factors may not strongly influence BC risk in this cohort. However, marital status was significantly associated with BC, with a higher proportion of cases being married. This finding warrants further investigation, as some studies suggest that marital status may influence cancer risk through factors like reproductive history, socioeconomic status, and access to healthcare.

The logistic regression analysis identified several lifestyle factors as significant predictors of BC risk. The use of oral contraceptive pills (OR=20.002), positive family history (OR=18.472), and smoking (OR=14.873) were the strongest risk factors. These findings are consistent with **Barańska & Kanadys, (2022)**, who reported that current oral contraceptive use was associated with a higher risk for invasive BC, and **Scala et al. (2023)**, who found that breast cancer risk increased linearly with the intensity and duration of smoking. The study also identified physical inactivity and CYP17 polymorphism as significant predictors, with ORs of 10.197 and 7.115, respectively. These findings align with **Verdiesen et al. (2025)**, who reported that increased height and decreased BMI are probable causal risk factors for all five BC subtypes, and **Ebrahimi et al. (2020)**, who found an association between CYP17 gene polymorphism and BC in Iranian women.

Moderate but significant contributions were observed from saturated fat intake (OR=6.152), emotional dissatisfaction (OR=2.361), and low sex satisfaction (OR=1.631). These psychosocial and dietary factors have been less extensively studied but are gaining attention in BC research. The association with emotional dissatisfaction and low sex satisfaction suggests that psychological well-being may influence cancer risk, as supported by emerging literature on the psychosocial determinants of health.

Study Limitations

Despite the comprehensive analysis, several limitations should be acknowledged. First, the case-control design is inherently susceptible to recall and selection biases, particularly regarding self-reported lifestyle, dietary, and psychosocial factors. Second, the study was conducted within a specific regional and socio-cultural context, which may limit the generalizability of findings to broader populations. Third, genetic analyses were restricted to selected polymorphisms (CYP17 and

CYP19), potentially overlooking other relevant genetic variations influencing breast cancer risk. Additionally, some potential confounders, such as environmental exposures and detailed hormonal profiles, were not assessed. Finally, cross-sectional measurement of psychosocial factors limits causal interpretation.

Conclusion

This study provides valuable insights into the multifactorial nature of BC risk among women under 50. The findings underscore the importance of considering a wide range of factors, including age, socio-demographic characteristics, medical history, reproductive history, and lifestyle behaviors, in BC risk assessment and prevention strategies. The consistency of these results with recent literature highlights the robustness of the identified risk factors, while the observed differences in some areas suggest the need for further research to understand the complex interactions influencing BC risk. Future studies should aim to explore these factors in greater depth, considering the specific socio-economic and cultural contexts that may modulate BC risk.

Study Recommendations

Based on the findings, several recommendations can be proposed. First, targeted awareness and educational programs should be implemented, emphasizing modifiable risk factors such as smoking cessation, physical activity, and dietary habits to reduce breast cancer incidence. Second, healthcare providers should integrate comprehensive risk assessments, including family history, hormonal exposure, and genetic screening for high-risk polymorphisms like CYP17, into routine clinical practice. Third, psychosocial well-being should be addressed as part of holistic prevention strategies, given the observed associations with emotional dissatisfaction and low sexual satisfaction. Finally, future research should adopt longitudinal designs, include broader genetic profiling, and explore environmental and socio-cultural influences to enhance risk prediction and prevention strategies

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