Association of Occupational and Lifestyle Factors with Mammography-Detected Breast Neoplasia

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Abstract

Background: Breast cancer is the most common malignancy affecting women, with higher mortality and morbidity. The early identification and diagnosis are the cornerstone of successful treatment and reduction of morbidity and mortality. Mammography is the gold standard screening tool. This work is designed to investigate the potential association between breast cancer and environmental factors related to lifestyle.

Methods: A cross-sectional study was done by collecting data from medical records of patients diagnosed with early diagnosed and well-established diabetes mellitus attending our university hospital; 300 women were screened by mammography for breast cancer. Women with positive results were assigned as the study group (n=39), while women with negative results were assigned as the control group (n=261). All were evaluated by the standard clinical approaches, and a pre-prepared questionnaire was used to collect data about social, environmental, and lifestyle factors. The collected data were submitted to statistical analysis using the Statistical Package for Social Science for Windows, version 20 (IBM, Chicago, USA).

Results: There was significant increase (*P*<0.001) of body mass index, hormone replacement therapy, age at first and last deliveries age at last baby and wearing tight bra; while there was significant decrease (*P*<0.001) of menarche, number of living children, mean age of weaning, and breast feeding in the study than the control group. In addition, there was significant increase (*P*<0.001) of long duration or night shift work, exposure to dangers at work, passive smoking, and use of kohl, drugs, crowding index, old painting, non-cemented ground, TV at bed rooms, pesticide exposure in the study than the control group. With multiple regression analysis, the early menarche, use of hormone replacement therapy, older age at first or last delivery, number of living children, mean age at weaning, breast feeding, tight bra, exposure to dangers at work, passive smoking, use of cosmetics (kohl), persons at home and crowding index remains the significant (*P*<0.001) associates with detected breast cancer.

Conclusion: This study used mammography as the gold-standard detection tool to identify neoplasia cases and analyze their association with environmental and occupational risk factors.

Keywords: Breast Cancer, Mammography, Shift work, Nulliparity, Breastfeeding

Introduction

Breast cancer is one of the oldest known forms of cancer.

In addition, it is the most common cancer and the cause of

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↑*What is "already known" in this topic:*
Breast cancer is the most common malignancy in women globally, with early detection critical to reducing mortality. While mammography's role in early detection and established risk factors (e.g., HRT, obesity) are well-documented, evidence remains scarce for environmental/occupational exposures in resource-limited settings. Controversial factors (e.g., tight bras, kohl use) and their interactions with classic risks are poorly understood.

→*What this article adds:*
This study addresses these gaps by analyzing multifactorial associations in a population underrepresented in prior research." The development of breast cancer is linked to numerous factors. Using mammography as a screening technique is an effective method for early detection of breast cancer, which is linked to a better prognosis.

death among females. Its incidence and related mortality witnessed a progressive reduction in high-resource countries. However, the incidence and related mortality are increasing in low-resource nations. This pattern is explained by the change in the profile of risk factors and access to facilities for early breast cancer detection and treatment. The known risk factors include advanced age, pattern of menarche, race, pattern of reproduction, hormonal use, characteristics of the breast, physical activity, body composition, and smoking or alcohol use (1).

Family history as a risk factor for breast cancer is a debatable issue. It had been believed that family history cannot be considered a risk factor for breast cancer, as 90% of women who developed breast cancer have a negative family history. This is attributed to environmental and lifestyle factors. However, others reported a strong risk relation between family history and breast cancer. There was a two-fold increase in the risk for women with positive family history in their first-degree family, especially if first-degree relatives developed cancer before the age of 50 years (2-4).

Exposure to environmental chemicals and pollutants (e.g., plastics, cosmetics, cleaning products, and pesticides) is increasing, and it may lead to the development of different diseases throughout our lives, especially with the presence of persistent organic pollutants (POPs) due to bioaccumulation in the food chain and environmental persistence. Evidence exists about the role of exposure to high or low-dose levels of some pollutants in the development of cancer or cancer progression (5). In addition, increasing evidence exists regarding the possible association between increased risk of breast cancer and certain ways of living, exposing the subject to certain risk factors. For example, a healthy lifestyle and breastfeeding are considered strongly associated factors with the prevention of breast cancer. Another study reported that physical activity is associated with risk reduction of breast cancer (6, 7).

Screening for breast cancer refers to testing healthy women for breast cancer, aiming to detect breast cancer in early phases when it is still curable to achieve a better prognosis and reduce cancer-specific risk of mortality. It is usually performed by mammography and other imaging modalities to detect any abnormal masses or lumps in the breast (8, 9).

The current work was designed to assess the potential role of mammography in early detection of any neoplastic changes of the breast that could be related to environmental or lifestyle factors. We believe that this will share in the understanding and reduction of breast cancer morbidity and mortality among women.

Methods
Type of study
This study was designed as a cross-sectional study, which included 300 women who fulfilled the inclusion criteria during the duration of the study (from September 2022 to August 2024).

Sample Size Calculation
The sample size was calculated using the formula for case-control studies:

$$n = \frac{(Z\alpha/2 + Z\beta)2 \times p(1-p)(r+1)}{d2 \times r}$$

Assumptions:
- Power (ZβZβ) = 80% (1.96 for α = 0.05).
- Odds ratio (OR) = 2.0 (based on prior studies for key exposures like hormone therapy).
- Prevalence of breast neoplasia (pp) = 5% (from regional screening data).
- Ratio of controls to cases (rr) = 4:1.
- Margin of error (dd) = 5%.
- Software: OpenEpi (version 3.01) was used for validation.
- This yielded a minimum required sample of 270 participants; we enrolled 300 to account for attrition.

The inclusion and exclusion criteria
Participants were consecutively enrolled from a standardized mammography screening program in our university hospital to minimize referral bias.

The exclusion criteria were females younger than 18 years of age, females previously treated with hormonal or radiation therapy, females with positive family history in the first-degree relatives, lactating females, and women with traumatic lesions of the breast. Family history was excluded to reduce confounding by genetic predisposition, allowing clearer analysis of environmental/lifestyle factors.

After proper consent, all women were evaluated by exhaustive clinical examination by the aid of gynecologists in the sitting and supine positions by inspection and palpation in a systematic manner, followed by mammography using Fujifilm Mammogram Imaging Solutions for Healthcare Systems in the diagnostic radiology department. Before mammography, patients were advised not to use any deodorant, powders, or ointments under their arms on the day of examination. All jewelries were removed from the neck and chest area. On examination, one breast was rested on a flat surface containing the x-ray plate, and a compressor was pressed firmly against the breast, and x-ray pictures were obtained from several angles after the patient held her breast. The obtained views included cranio-caudal (top to bottom), Medio-lateral oblique (MLO), and "Spot" views.

Grouping: Women were categorized into two groups according to the results of mammography. The positive group included females with suspected neoplastic changes (39 women), and the negative group included women free from any suspected pathological lesions (261), and they are marked as the control group.

Regardless of the results of mammography, all women complete a preformed Validated questionnaire items (adapted from the WHO STEPS survey and Breast Cancer Surveillance Consortium) were used to standardize self-reported data to collect their demographic (age, age of menarche, age of first pregnancy and getting first child, number of live children, breast feeding), life style and exposure to environmental health hazard (e.g., electromagnetic field exposure, video display terminals. Television in bedrooms, mobile phone usage, charging electronic household utensils such as vacuum cleaners, washing machines, etc, in addi-

tion to the site, duration, and frequency of exposure. Pesticide use (types, frequency, duration, direct or indirect exposure). Special habits (e.g., smoking, perfumes, aromatic sticks, use of cosmetics and hair coloring agents). In addition, the crowding index (CI) was calculated as the total surface area of the building divided by the number of persons occupying the building. Sexual life and manipulations. The data about dietary habits were also collected (e.g., consumption of fats, fruits, and vegetables), clothing (nature, duration of wearing, and its materials), work (hours, shifts, and environmental risk exposure at the site of work). Variables like age, BMI, and parity were included in multivariate logistic regression models.

Data analysis: The collected data were organized, tabulated, and analyzed using SPSS version 24, (SPSS Inc., USA). Quantitative data were represented as mean and standard deviation (SD), while qualitative data (categorical) were represented as frequency and percent distribution. Student (t) test and chi-square (X^2) test used as tests of significance for quantitative and qualitative data, respectively. For interpretation of results, p p-value < 0.05 was considered significant.

Logistic regression was performed with mammography result (positive/negative) as the binary outcome variable.

Results are presented as adjusted odds ratios (ORs) with 95% confidence intervals, controlling for age, BMI, and socioeconomic status. Variables were selected for the final model based on univariate screening ($P<0.20$).

Results

There were 560 screening mammograms in 300 women; 261 were of normal cases, and 39 were diagnosed with neoplastic changes of the breast (Figure 1).

Sociodemographic data and significant environmental factors

In the present study, there was significant increase of BMI, HRT, age at first baby, age at last baby, wearing tight bra and synthetic bra materials; while there was significant decrease of menarche, number of living children, mean age of weaning, and breast feeding in the study than the control group (Table 1). In addition, there was a significant increase in long duration or night shift work, exposure to dangers at work, passive smoking, and use of kohl, drugs, crowding index, old painting, non-cemented ground, and TV in bedrooms in the study than the control group (Table 2).
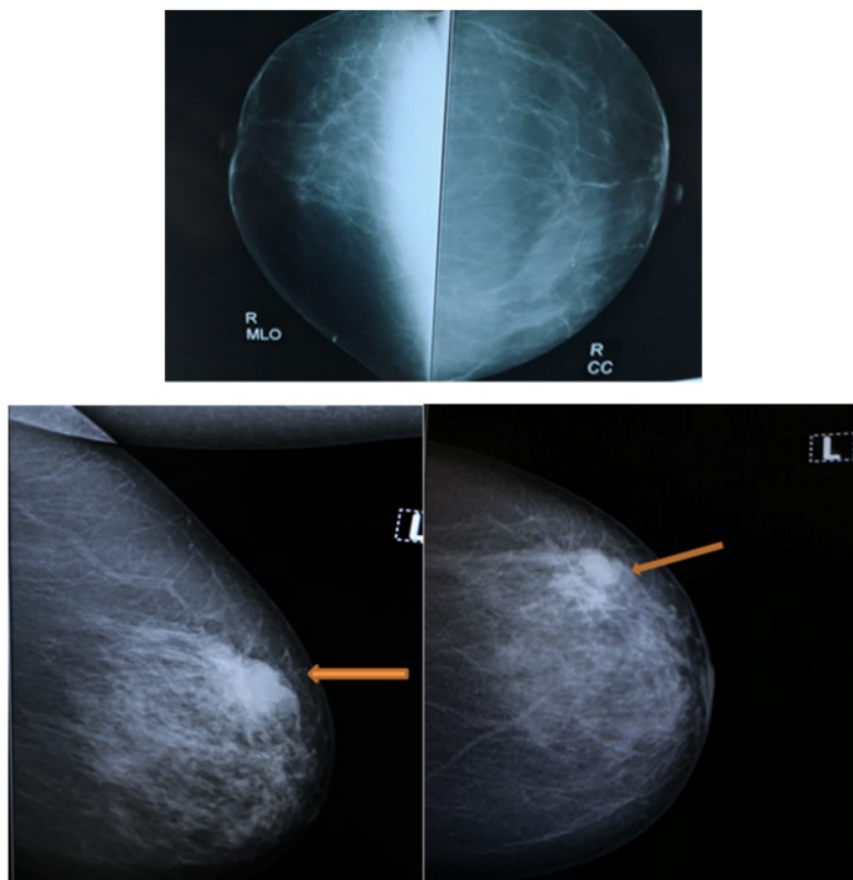

Figure 1. A: Female 41 y, complaining of nipple and retroareolar pain. Mammography findings showed a normal mammogram, fatty breast, and no definite calcification was seen. This case is categorized as BIRAD 1. B: Female 57y, complaining of hard breast mass, no positive family history. The Mammography findings at the left breast are: Mass (arrow) with irregular shape seen at upper outer quadrant: Spiculated margin, High density, surrounding distorted high-density soft tissues, no calcification seen. This mass is categorized as BI-RADS 5.

Table 1. Comparison between study and control groups with regard to significant sociodemographic data

Variable	Study (n=39)	Control (n=261)	P value
Age (year)	51.08±3.72; 44-59	50.66±3.07; 44- 59	0.450
Weight (kg)	79.18±5.42; 69- 91	72.29±5.86; 59- 89	<0.001*
Height (cm)	163.87±5.45; 152- 180	164.26± 4.98; 152-180	0.610
Body mass index (kg/m^2)	29.55±2.56	26.87±2.73	<0.001*
Age at Menarche (year)	11.31±0.77; 10- 13	11.69±0.95; 10- 14	0.016*
Hormone replacement therapy (n, %)	16 (41.0%)	15 (5.7%)	<0.001*
Age at first delivery (year)	26.13±2.19; 21-30	24.24±1.32; 20-29	<0.001*
Age at last delivery (year)	38.18±1.65; 34 – 42	33.56±2.00; 28- 39	<0.001*
Number of living children	2.08±0.62; 1-3	2.52±0.67; 1-4	<0.001*
Mean age of weaning (months)	14.18±5.15; 6- 28	18.32±4.39; 10-24	<0.001*
Breastfeeding (n, %)	15(38.5%)	220(84.3%)	<0.001*
Wearing a Tight bra (n, %)	20(51.3%)	12(4.6%)	<0.001*
Synthetic bra material (n,%)	17(43.6%)	15(5.7%)	<0.001*

*Significant at the level of α=0.05

Table 2. Comparison between study and control groups with regard to significant environmental factors

Variable	Study (n=39)	Control (n=261)	P value
Long duration of work (n,%)	29(74.4%)	96(36.8%)	< 0.001*
Exposure to dangers (n,%)	22(56.4%)	26 (10.0%)	0.001*
Active smoking (n,%)	2(5.1%)	6(2.3%)	0.310
Passive smoking (n,%)	27 (69.2%)	27 (10.3%)	<0.001*
Active/or passive smoking (n,%)	29 (74.4%)	33 (12.6%)	<0.001*
Use of cosmetics (kohl) (n,%)	22 (56.4%)	36 (13.8%)	<0.001*
Drugs for chronic disease (s) (n,%)	23(59.0%)	96(36.8%)	0.008*
Persons/home	4.82±1.27; 2-7	4.10±0.94; 2-6	<0.001*
Crowding index	3.61±1.18; 2-7	2.53±0.68; 2-6	<0.001*
Old paint (n,%)	10 (25.6%)	25 (9.6%)	0.004*
Uncemented ground (n,%)	16(41.0%)	37 (14.2%)	<0.001*
TV in bedroom (n,%)	5 (12.8%)	10 (3.8%)	0.016*
Long-term exposure to pesticides	14 (35.9%)	38 (14.6%)	0.002*

*Significant at the level of α=0.05

Table 3. Logistic Regression Analysis of Factors Associated with Mammography-Detected Breast Neoplasia (N=300)

Variable		Adjusted OR	95% CI	P-Value
Reproductive Factors	Age at menarche (per year)	1.03	1.01-1.05	0.005*
	HRT use (yes vs no)	1.17	1.10-1.25	<0.001*
	Age at first delivery (per year)	1.02	1.00-1.03	0.026*
	Age at last delivery (per year)	0.95	0.93-0.97	<0.001*
	Number of living children	1.09	1.04-1.14	<0.001*
	Breastfeeding (yes vs no)	0.90	0.86-0.95	<0.001*
Lifestyle Factors	Tight bra use (yes vs no)	1.24	1.14-1.35	<0.001*
	Passive smoking (yes vs no)	1.08	1.02-1.15	0.007*
	Kohl use (yes vs no)	1.13	1.07-1.19	<0.001*
Environmental Factors	Workplace hazard exposure	1.17	1.11-1.24	<0.001*
	Crowding index	0.94	0.91-0.97	<0.001*

P<0.05, OR > 1 indicates increased risk, OR < 1 indicates protective effect

Running Logistic regression analysis, the early menarche, use of hormone replacement therapy, older age at first or last delivery, number of living children, mean age at weaning, breast feeding, tight bra, exposure to dangers at work, passive smoking, use of cosmetics (kohl), persons at home and crowding index remains significant associates with detected breast cancer (Table 3).

Discussion

As there is a consensus that mammography is the gold-standard screening tool for early detection of breast cancer (10, 11), we used it as the screening tool in the current work. Our subjects were divided according to the results of the mammography: the positive (study) and negative (control) group. The mammographic screening detected suspicious lesions among 39 women (14.9%). Results also showed that the development of mammographic changes indicating breast cancer is associated with increased body mass index, which remains significantlyassociated after multiple regression analysis. These results are in line with previous studies. For example, Key et al. (12) and Yaghjyan et al. (13) reported that obese women are at greater risk for the development of breast cancer, and there was an inverse correlation between body mass index and breast density. A recent meta-analysis included more than 2.5 million women investigating the possible association between breast cancer and body mass index, revealing that the risk of breast cancer is reduced by 8% for every 5 kg/m² decrease in BMI (14).

Different mechanisms are responsible for the increased breast cancer risk (increased density) among obese women. For example, the reduced levels of estradiol in premenopausal women, which worked as a potent stimulator for breast tissue proliferation (both for epithelial and stromal tissue) (15, 16). In addition, Garcia-Estevez et al. (14) reported that potential mechanisms linking obesity to breast cancer include the role of estrogens, insulin resistance, and chronic inflammation.

The results of the current work showed that the detection of breast cancer is associated with precocious puberty (early menarche). This remains significant with multiple regression analysis. These results are comparable to

Hadjisavvas et al. (17) reported that women starting to menstruate early (especially below 11 years of age) had a greater risk for breast cancer than women who menstruated at a later age. In addition, a positive association between the younger age of menarche and density of breast tissues, especially in premenopausal women (18). This link is in line with the hypothesis that the risk of breast cancer is associated with the extent of breast mitotic activity. This activity is regulated by estrogen and progesterone during the luteal phase of the menstrual cycle, which determines the probability of tumorigenic somatic events (19). Therefore, an early age at menarche increases the duration of mitotic activity in the breast and thus increases the risk of breast cancer.

Women receiving hormone replacement therapy (HRT) are significantly more likely to be in the study than the control group. This agrees with Beral et al. (20) and Harlid et al. (21) who reported that HRT increased the risk of breast cancer and the combination of HRT and duration of therapy are determinant factors in this risk. They also reported a marked association between HRT and genetic risk factors for the development of breast cancer.

Women with mammographic findings suggestive of breast cancer had significantly higher ages of the first and last deliveries, with significantly lower number of living children, early weaning, and significant reduction of breastfeeding. All associations remained significant after multiple regression analysis. These results agree with Kawase et al. (22), who found a higher risk of breast cancer in nulliparous women and for women giving birth to few children (one or two). On the other hand, the study by Travis et al. (23) did not find any significant association between the risk of breast cancer and parity and age of first childbirth. In addition, Milne et al. (24) reported that no significant link was seen between parity and age at first childbirth. A possible explanation for this contradiction may be related to the fact that these studies investigated the association between specific genetic factors and environmental factors that can be different than the disease diagnosis by mammography in the present study.

The effect of breastfeeding on the risk of breast cancer has been controversial. Some researchers reported no associations, while others reported a protective action of breastfeeding against breast cancer. Lipworth et al. (25) reported that the studies showing the protective effect of breastfeeding are usually from countries with a long duration of breastfeeding. However, this association could not be confirmed in Western countries. They attributed this to the low prevalence of long-duration breastfeeding in Western countries. However, Hadjisavvas et al. (17) reported that pregnancy and breastfeeding reduced the risk of breast cancer. In addition, Jordan et al. (26) reported that pregnancy and long-standing lactation are associated with a lower breast cancer risk than pregnancy alone.

Wearing a tight bra and synthetic material of the bra are significantly associated with breast cancer. However, with multiple linear regression, the tight bra remains significant while the synthetic bra shows a non-significant association. Kramer et al. (27) reported that, tight bra is associated with increased risk for breast cancer and they traced the literature to first reporting of this fact and reached the year 1995 with publication of a boot titled "Dress to kill" where authors claimed that the women wearing tight-fitting bras all day, every day had a higher risk for breast cancer development than other women who do not practice the same pattern. They explained higher risk by inhibition of lymphatic drainage with trapping of toxins caused by a tight bra. However, this theory has not been widely accepted, and other confounding variables may play a role significant than tight bra. This is accepted as the disease is now attributed to many risk factors (as found in the current work).

The environment of the work is also associated with a significant increase in the risk of development of breast cancer. For example, long duration of work, night shifts, and exposure to dangers (especially chemicals) are significantly increased in the study group compared to the control group. This was in line with previous studies of Straif et al. (28) and Kolstad et al. (29) who reported that the shift work includes disruption of circadian rhythm is probably a carcinogen to humans. However, multiple regression analysis only confirmed the exposure to dangers as a risk for the development of breast cancer. This could be attributed to the small number of women who had shifts or a long duration of work.

Passive smoking was significantly associated with the development of breast cancer and remained significant after multiple regression analysis. This could be attributed to carcinogens in smoke that increased the risk of breast cancer. This is significantly related to the duration and density of smoking (30). A more recent study also confirmed the hazard of active smoking on the risk of breast cancer (31). However, this could not be confirmed in the current work due to the minority of women who actively smoke. Ellingjord-Dale et al. (32) concluded that smoking, physical activity, and alcohol drinking are associated with breast cancer (especially Luminal A-Like type).

The use of traditional cosmetics (Kohl), old paintings, and uncemented floors was significantly increased in the study group than the control group. Only the use of kohl remains significant after multiple regression. The carcinogenic effects of the traditional cosmetics could be related to their contents of heavy metal (lead). This fact is confirmed in experimental studies, as lead promotes the development of mammary tumors and accelerates the rate of tumor growth. This was confirmed by higher levels of lead in the hair samples of newly diagnosed women with breast cancer (all were of ductal carcinoma) (33).

TV in bedrooms and pesticide exposure were significantly higher in the study than in the control group. However, this association did not stand with multiple regression analysis. This association was reported by Davis et al. (34) and O'Leary et al. (35), and they attributed increased risk of cancer to the presence of ambient light in the bedroom. Light at night in the bedroom may reduce the melatonin production, with increased estrogen production that increases the risk of breast cancer (36). Other suggested

mechanisms involve the alteration of clock gene function and desynchronization of the master clock from the peripheral clocks (37).

Overall results of the current study agree with Boada et al. (38) who reported that early menarche, late age at first pregnancy, Nulliparity, lactation, years of reproductive life, hormonal contraception, and hormone replacement therapy have been associated to an estrogenic environment and increased risk of breast cancer.

Limitations of the study

This study has several limitations: First, its cross-sectional design precludes causal inference, and longitudinal studies are needed to confirm temporal relationships. Second, the exclusion of women with a family history of breast cancer limits generalizability to genetically predisposed populations. Third, while the sample size was adequate for preliminary exploration of risk factors, larger cohorts are required to validate rare exposures. Fourth, self-reported data on lifestyle factors may introduce recall bias, and genetic/dietary confounders were not assessed. Finally, controversial associations (e.g., tight bras, kohl use) warrant mechanistic investigation, as our findings align with regional practices but lack biological corroboration."

Conclusion

This study identified several environmental and lifestyle factors associated with mammography-detected breast neoplasia, including occupational hazards, reproductive history, and regional practices. It also highlights the crucial role of mammography in early disease detection, but future studies should integrate these risk factors into risk prediction models to refine screening strategies for high-risk populations.

Authors' Contributions

"Conceptualization, A.A and H.E.; methodology, A.A and H.E.; software, A.A and H.E.; validation, A.A and H.E.; formal analysis, A.A and H.E.; investigation, A.A and H.E.; data curation, A.A and H.E.; writing original draft preparation, A.A and H.E.; writing review and editing, A.A and H.E.; visualization, A.A and H.E.; supervision, A.A and H.E.; project administration, A.A and H.E.; All authors have read and agreed to the published version of the manuscript..

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of Damietta Faculty Of Medicine, Al-Azhar University (DFM-IRB 00012367-24-09-009)." for studies involving humans.

Acknowledgment
None.

Conflict of Interests
The authors declare that they have no competing interests.

References
1. Winters S, Martin C, Murphy D, Shokar NK. Breast Cancer Epidemiology, Prevention, and Screening. Prog Mol Biol Transl Sci. 2017;151:1-32.
2. Barnard ME, Boeke CE, Tamimi RM. Established breast cancer risk factors and risk of intrinsic tumor subtypes. Biochim Biophys Acta. 2015 Aug;1856(1):73-85.
3. Bashamakha G, Bin Sumait H, Bashamakha M, Al Serouri A, Khader Y. Risk Factors of Breast Cancer in Hadramout Valley and Desert, Yemen. Int J Prev Med. 2019 Oct 9;10:161.
4. Liu R, Kitamura Y, Kitamura T, Sobue T, Sado J, Sugawara Y, et al. Three-Prefecture Cohort Study Group. Reproductive and lifestyle factors related to breast cancer among Japanese women: An observational cohort study. Medicine (Baltimore). 2019 Dec;98(51):e18315.
5. Koual M, Tomkiewicz C, Cano-Sancho G, Antignac JP, Bats AS, Coumoul X. Environmental chemicals, breast cancer progression and drug resistance. Environ Health. 2020 Nov 17;19(1):117.
6. Inumaru LE, Silveira EA, Naves MM. [Risk and protective factors for breast cancer: a systematic review]. Cad Saude Publica. 2011 Jul;27(7):1259-70.
7. Gao Y, Huang YB, Liu XO, Chen C, Dai HJ, Song FJ, et al. Tea consumption, alcohol drinking and physical activity associations with breast cancer among Chinese females: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2013;14(12):7543-50.
8. Coleman C. Early Detection and Screening for Breast Cancer. Semin Oncol Nurs. 2017 May;33(2):141-155.
9. Niell BL, Freer PE, Weinfurtner RJ, Arleo EK, Drukteinis JS. Screening for Breast Cancer. Radiol Clin North Am. 2017 Nov; 55(6):1145-1162.
10. Vachon CM, Brandt KR, Ghosh K, Scott CG, Maloney SD, Carston MJ, et al. Mammographic breast density as a general marker of breast cancer risk. Cancer Epidemiol Biomarkers Prev. 2007 Jan;16(1):43-9.
11. Ginsburg OM, Martin LJ, Boyd NF. Mammographic density, lobular involution, and risk of breast cancer. Br J Cancer. 2008 Nov 4;99(9):1369-74.
12. Key TJ, Verkasalo PK, Banks E. Epidemiology of breast cancer. Lancet Oncol. 2001 Mar;2(3):133-40.
13. Yaghjyan L, Mahoney MC, Succop P, Wones R, Buckholz J, Pinney SM. Relationship between breast cancer risk factors and mammographic breast density in the Fernald Community Cohort. Br J Cancer. 2012 Feb 28;106(5):996-1003.
14. Garcia-Estevez L, Cortés J, Pérez S, Calvo I, Gallegos I, Moreno-Bueno G. Obesity and breast cancer: a paradoxical and controversial relationship influenced by menopausal status. Front Oncol. 2021;11:705911.
15. Onland-Moret NC, Peeters PH, van der Schouw YT, Grobbee DE, van Gils CH. Alcohol and endogenous sex steroid levels in postmenopausal women: a cross-sectional study. J Clin Endocrinol Metab. 2005 Mar;90(3):1414-9.
16. LaMarca HL, Rosen JM. Estrogen regulation of mammary gland development and breast cancer: amphiregulin takes center stage. Breast Cancer Res. 2007;9(4):304.
17. Hadjisavvas A, Loizidou MA, Middleton N, Michael T, Papachristoforou R, Kakouri E, et al. An investigation of breast cancer risk factors in Cyprus: a case control study. BMC Cancer. 2010 Aug 23;10:447.
18. El-Bastawissi AY, White E, Mandelson MT, Taplin SH. Reproductive and hormonal factors associated with mammographic breast density by age (United States). Cancer Causes Control. 2000 Dec;11(10):955-63.
19. Dumitrescu RG, Cotarla I. Understanding breast cancer risk -- where do we stand in 2005? J Cell Mol Med. 2005 Jan-Mar;9(1):208-21.
20. Beral V, Banks E, Reeves G. Evidence from randomised trials on the long-term effects of hormone replacement therapy. Lancet. 2002 Sep 21;360(9337):942-4.
21. Harlid S, Butt S, Ivarsson MI, Eyfjörd JE, Lenner P, Manjer J, et al. Interactive effect of genetic susceptibility with height, body mass index, and hormone replacement therapy on the risk of breast cancer. BMC Womens Health. 2012 Jun 22;12:17.
22. Kawase T, Matsuo K, Suzuki T, Hiraki A, Watanabe M, Iwata H, et al. FGFR2 intronic polymorphisms interact with reproductive risk factors of breast cancer: results of a case control study in Japan. Int J Cancer. 2009 Oct 15;125(8):1946-52.
23. Travis RC, Reeves GK, Green J, Bull D, Tipper SJ, Baker K, et al Million Women Study Collaborators. Gene-environment interactions in 7610 women with breast cancer: prospective evidence from the Million

Women Study. Lancet. 2010 Jun 19;375(9732):2143-51.

24. Milne RL, Gaudet MM, Spurdle AB, Fasching PA, Couch FJ, Benítez J, , et al. Assessing interactions between the associations of common genetic susceptibility variants, reproductive history and body mass index with breast cancer risk in the breast cancer association consortium: a combined case-control study. Breast Cancer Res. 2010;12(6):R110.

25. Lipworth L, Bailey LR, Trichopoulos D. History of breast-feeding in relation to breast cancer risk: a review of the epidemiologic literature. J Natl Cancer Inst. 2000 Feb 16;92(4):302-12.

26. Jordan I, Hebestreit A, Swai B, Krawinkel MB. Breast cancer risk among women with long-standing lactation and reproductive parameters at low risk level: a case-control study in Northern Tanzania. Breast Cancer Res Treat. 2013 Nov;142(1):133-41.

27. Kramer SM. Fact or Fiction? Underwire Bras Cause Cancer, April 19, 2007. Available at https://www.scientificamerican.com/article/fact-or-fiction-underwire-bras-cause-cancer/. Last accessed May 2020

28. Straif K, Baan R, Grosse Y, Secretan B, El Ghissassi F, Bouvard V, et al WHO International Agency For Research on Cancer Monograph Working Group. Carcinogenicity of shift-work, painting, and fire-fighting. Lancet Oncol. 2007 Dec;8(12):1065-6.

29. Kolstad HA. Nightshift work and risk of breast cancer and other cancers--a critical review of the epidemiologic evidence. Scand J Work Environ Health. 2008 Feb;34(1):5-22.

30. Band PR, Le ND, Fang R, Deschamps M. Carcinogenic and endocrine disrupting effects of cigarette smoke and risk of breast cancer. Lancet. 2002 Oct 5;360(9339):1044-9.

31. Xue F, Willett WC, Rosner BA, Hankinson SE, Michels KB. Cigarette smoking and the incidence of breast cancer. Arch Intern Med. 2011 Jan 24;171(2):125-33.

32. Ellingjord-Dale M, Vos L, Hjerkind KV, Hjartåker A, Russnes HG, Tretli S, et al. Alcohol, Physical Activity, Smoking, and Breast Cancer Subtypes in a Large, Nested Case-Control Study from the Norwegian Breast Cancer Screening Program. Cancer Epidemiol Biomarkers Prev. 2017 Dec;26(12):1736-1744.

33. Florea AM, Büsselberg D. Metals and breast cancer: risk factors or healing agents? J Toxicol. 2011;2011:159619.

34. Davis S, Mirick DK, Stevens RG. Night shift work, light at night, and risk of breast cancer. J Natl Cancer Inst. 2001 Oct 17;93(20):1557-62.

35. O'Leary ES, Schoenfeld ER, Stevens RG, Kabat GC, Henderson K, Grimson R, et al. Electromagnetic Fields and Breast Cancer on Long Island Study Group. Shift work, light at night, and breast cancer on Long Island, New York. Am J Epidemiol. 2006 Aug 15;164(4):358-66.

36. Stevens RG, Blask DE, Brainard GC, Hansen J, Lockley SW, Provencio I, et al. Meeting report: the role of environmental lighting and circadian disruption in cancer and other diseases. Environ Health Perspect. 2007 Sep;115(9):1357-62.

37. Hoffman AE, Zheng T, Yi CH, Stevens RG, Ba Y, Zhang Y, et al. The core circadian gene Cryptochrome 2 influences breast cancer risk, possibly by mediating hormone signaling. Cancer Prev Res (Phila). 2010 Apr;3(4):539-48.

38. Boada LD, Zumbado M, Henríquez-Hernández LA, Almeida-González M, Alvarez-León EE, Serra-Majem L, et al. Complex organochlorine pesticide mixtures as determinant factor for breast cancer risk: a population-based case-control study in the Canary Islands (Spain). Environ Health. 2012 Apr 25;11:28.