ONLINE FIRST

ORIGINAL ARTICLE

Early-Age Breast Cancer during Active Conflict in Syria: A Cross-Sectional Study

Yahya A. Mutair[1], Gohar Mushtaq[2*] Fouad Al-Daoud[3], Maryam Al-Qassim[4], Mahmoud Hariri[5]

[1]*Department of Surgery, Faculty of Medicine, Idlib University, Idlib, Syria*
[2]*Center for Scientific Research, Faculty of Medicine, Idlib University, Idlib, Syria*
[3]*Department of Laboratory Diagnosis, Faculty of Medicine, Idlib University, Idlib, Syria*
[4]*Department of Breast Cancer Screening, Idlib Oncology Center, Idlib, Syria*
[5]*Department of Surgery, Syrian Board of Medical Specialties, Gaziantep, Turkey*
Correspondence: *dr.goher_mushtaq@idlib-university.com*
doi: 10.22442/jlumhs.2024.01096

ABSTRACT

OBJECTIVE: To examine the risk factors associated with breast cancer within a war-affected region enduring over a decade of conflict in Northwest Syria.
METHODOLOGY: A cross-sectional study was conducted from January to December 2022. Inclusion criteria required patients to have a palpable breast mass confirmed by biopsy. Patients residing in the region for less than 5 years were excluded from the study. The study included 164 female patients, averaging 47.14±11.31 years. Data were collected through surveys during visits to the regional cancer center. Ten risk factors were analyzed: Age, family history, Age at menarche, age at menopause, body mass index, breastfeeding, age at first birth, smoking, hormonal contraceptive use, and psychological stress. Statistical analysis was performed using IBM SPSS Statistics 25.
RESULTS: Among the breast cancer patients, 32.9% were ⩽40 years old (mean = 34.7, SD = 4.35), 32.9% were 41-50 years old (mean = 46.3, SD = 2.75), and 34.1% were >50 years old (mean = 59.89, SD = 6.15). Significant correlations ($p < 0.05$) were found between all fixed and variable risk factors except smoking, age at menarche, and hormonal contraceptive use.
CONCLUSION: Our study revealed a nearly ten-year decrease in the average age of breast cancer onset among our patients compared to global standards. Prolonged conflict is likely a key factor driving earlier and increased breast cancer cases in Syria's younger women. These findings highlight the need for targeted public health interventions and further research into the impact of chronic conflict on cancer epidemiology.

KEYWORDS: Breast cancer, early age, risk factors, stress, protracted conflict

INTRODUCTION

Breast cancer is prevalent in all countries. However, in war-ridden areas of protracted conflict, there is an increased prevalence of breast cancer owing to additional risk factors. Northwest Syrian liberated areas outside government control are one such example. Based on a study conducted in 2020, breast cancer was the most common cancer (38.3%) among women in this region of Syria, and it was the most prevalent cancer (20.2%) in the overall proportion of cancer diagnoses[1].

There are certain predisposing risk factors for breast cancer. Risk factors change the exposure of breast tissue to reproductive hormones[2]. Breast cancer risk rises with factors like older age, extended menstrual history (early onset or late menopause), nulliparity, giving birth after 30, and oral contraceptive use[3,4]. Age is one of the most critical risk factors for breast cancer. Most breast cancer cases and related deaths occur between the ages of 40-60 years[5].

Additionally, reproductive history remains a critical aspect of breast cancer risk. Nulliparity and having the first child after age 30 are established risk factors. Studies have shown that the protective effect of early full-term pregnancy might be related to the differentiation of breast cells, which reduces their susceptibility to carcinogenic mutations[6]. Moreover, breastfeeding has a protective effect, with longer durations of breastfeeding associated with a further reduction in breast cancer risk. A pooled analysis of 47 epidemiological studies found that for every 12 months of breastfeeding, the relative risk of breast cancer decreased by 4.3% [7].

Early puberty is a predisposing factor for breast cancer in females. Menstruation before age 12 elevates the risk of female breast cancer[8]. Likewise, patients who experience early menopause are shown to have a lower risk of breast cancer, while women who experience late menopause are more likely to develop breast cancer. For every year menopause is delayed beyond the age of 50, the incidence of breast cancer increases by 3% [9]. Furthermore, it has been shown that a delay in childbearing among women increases the incidence of breast cancer significantly if the childbearing age is delayed beyond the age of 30 [10].

The use of oral contraceptives for a period more extended than ten years increases the risk of breast cancer, mainly when using old monophasic contraceptives[11]. In addition, estrogen exposure, both endogenous and exogenous, plays a significant role in breast cancer development. Long-term hormone replacement therapy (HRT) has been associated with an increased risk of breast cancer, mainly when used for more than five years. A cohort study from the Women's Health Initiative found that women using combined estrogen-progestin HRT had a 24% increased risk of invasive breast cancer compared to non-users[12]. Genetic predispositions, such as mutations in the BRCA1 and BRCA2 genes, also significantly elevate the risk of breast cancer. Women with BRCA1 mutations have a 55-65% lifetime risk, while those with BRCA2 mutations have a 45% risk [13].

Lifestyle also has a profound impact on the development of risk factors for breast cancer[14]. Drinking alcohol in large quantities, at a rate of 35-44 grams of alcohol per day, is a predisposing factor for breast cancer, increasing the possibility of breast cancer by 32% [15]. Additionally, the diet pattern in developed countries that is rich in animal fats is considered a predisposing factor for breast cancer[16]. Smoking heightens breast cancer risk in female smokers, particularly in younger women[17]. Other risk factors for breast cancer include family history, increased body mass index, smoking, alcohol consumption, and dietary habits[18,19]. One large study that comprised 113,000 women from the general United Kingdom population showed that women

with two or more relatives with breast cancer had a 2.5 times higher risk for the incidence of breast cancer than women without such a family history[20].

External factors also play an essential role in increasing the risk of breast cancer. It has been shown that the rates of breast cancer converged among the descendants of immigrant women from lows-incidence countries who had settled in countries with a high incidence of breast cancer[21,22]. Both physical and psychological stresses stemming from daily stressors or familial loss-induced depression are essential to breast cancer risk factors[23]. Russian bombings, including chemical bombings in Idlib (Syria), caused destruction, toxic air pollution, and disrupted food production, with primitive oil refining and unlicensed pesticide use, as well as psychological stress due to bombings. Numerous early breast cancer reports prompted our first-of-its-kind cross-sectional study in Northwest Syria to investigate risk factors contributing to increased breast cancer among local women.

METHODOLOGY

A cross-sectional study design was used to examine the risk factors associated with breast cancer within a war-affected region enduring over a decade of conflict. This study was conducted between January and December 2022 at the sole regional cancer center in Northwest Syria, located in Idlib. The study included 164 biopsy-confirmed female breast cancer patients who had a palpable mass in the breast at the time of diagnosis.

Inclusion criteria required patients to have a palpable breast mass confirmed by biopsy who presented to the regional cancer center. Patients who resided in the Northwest Syria region for less than 5 years were excluded from this study.

Data were collected from patients through comprehensive surveys during their visits to the cancer center. Data were gathered through direct interviews using a unique form containing ten variables for all patients who visited the centre to receive chemotherapy. These variables included Age, family history, Age at menarche, age at menopause (nonmodifiable), body mass index, breastfeeding, age at first birth, smoking, hormonal contraceptive use, and psychological stress (modifiable). Each variable was categorized into three groups: high risk (assigned a score of 3), moderate risk (assigned a score of 2), and low or no risk (assigned a score of 1).

Statistical analysis was performed using IBM SPSS Statistics 25®, and graphs were created using Graph Pad Prism 7®. Descriptive statistics, including frequencies, means, medians, and standard deviations, were calculated, and Spearman correlation tests were conducted to examine the relationships between breast cancer risk factors. Additionally, Kruskal-Wallis tests were employed to explore associations between risk factors and breast cancer occurrence.

Risk factors for the study were based on the Gail Claus model and other established risk assessment factors[24]. (**Table I)**

The risk factors categorized for this study were as follows:

Table I: Risk Factors Categorized for the Study

Risk Factor	High Risk	Moderate Risk	Low Risk
Age	≤40 years	41-50 years	>50 years
Family History	First- and second-degree relatives	Third- and fourth-degree relatives	No family history
Puberty	<12 years	12-14 years	>14 years
Age at Menopause	>50 years	45-50 years	<45 years
First Pregnancy Age	Infertility	>20 years	≤20 years
Oral Contraceptive Usage	>5 years	2-5 years	<2 years
Smoking	One or more packets/day	Half a packet/day	Nonsmoking
Breastfeeding	No breastfeeding	<1 year breastfeeding	>1 year breastfeeding
Body Mass Index (BMI)	BMI >30	25-30	<25
Psychological Distress	Forced displacement or loss of a family member	Work loss due to war	No displacement or family loss

RESULTS

The results obtained from the statistical analysis are summarized and categorized in **Table II**. Age was identified as the most significant risk factor for breast cancer. The study included 164 patients aged between 24 and 75, averaging 47.14 years (SD = 11.31). Among these patients, 72% lacked a family history of breast cancer, while 26.8% had a history among first-, second-, or third-degree relatives. Notably, younger patients (⩽40 years old) generally had no family history of breast cancer. Breastfeeding was prevalent among the patients, with 78.7% having breastfed their children for more than one year, 0.6% breastfed for less than one year, and 20.7% did not breastfeed. Body Mass Index (BMI) analysis revealed that 23.2% of the patients had a BMI of less than 25, 31.7% had a BMI between 25-30, and 45.1% had a BMI greater than 30.

Puberty onset among patients varied, with 1.2% beginning menstruation before age 12, 50.6% between ages 13-14, and 48.2% after age 14. Menopause data showed that 70% of patients experienced early menopause or were under 45 and still menstruating, 15.9% stopped menstruating between ages 45-50, and 14.6% experienced late menopause. Regarding first pregnancy age, 45.2% had their first pregnancy before age 20, 40.2% after age 20, while 14.6% were infertile or childless, highlighting the impact of reproductive history on breast cancer risk. The majority of patients did not use hormonal contraceptives or used them for less than two years (78.7%), with 11.6% using them for 2-5 years and 9.8% using them for more than five years. Most patients were nonsmokers, with 87.8% never having smoked. Of the smokers, 3.7% consumed one pack per day, and 7.3% smoked more than one pack daily. Additionally, psychological distress was prevalent, with 71.4% of patients reporting moderate to severe stress, while 28.7% did not report any psychological distress.

Table II: Selected breast cancer risk factors

	Values	Frequency (N)	Percent (%)
AGE	<=40	54	32.9
	41-50	54	32.9
	>50	56	34.2
FAMILY HISTORY	NONE	118	721
	YES	46	28
BREASTFEEDING	MORE THAN 1 YEAR	129	78.7
	less than 1 year	1	0.6
	NONE	34	20.7
BODY MASS INDEX	<25	38	23.2
	25-30	52	31.7
	>30	74	45.1
AGE AT MENARCHE	> (14)YEARS	79	48.2
	(13-14)YEARS	83	50.6
	<(12)YEARS	2	1.2
AGE AT MENOPAUSE	MENSTRUATING/EARLY MENOPAUSE	115	70.1
	PERI-MENOPAUSE(45-50Y)	26	15.9
	DELAYED MENOPAUSE	23	14
AGE AT FIRST BIRTH	<20	74	45.1
	>20	66	40.2
	NULLIPAROUS	24	14.6
USE OF ORAL CONTRACEPTIVES	NO OR<2 YEARS	129	78.7
	2-5 YEARS	19	11.6
	>5 YEARS	16	9.8
SMOKING	NONE	144	87.8
	(1/2)PACKS/YEAR	6	3.7
	>=(1)PACKS/YEAR	14	8.5
STRESS	NO	47	28.7
	MILD	58	35.4
	SEVERE	59	36

Table III: Correlation coefficients between breast cancer risk and breast cancer risk factors

Variables	Age	Family history	Body mass index	Breastfeeding	Age at menarche	Age at menopause	Age at first birth	Use of oral contraceptives	Smoking	stress	Risk
Correlation Coefficient	.496	.363	.355	.430	0.106	.452	.290	0.110	.165	.373	
Sig. (2tailed)	0.0001	0.0001	0.0001	0.0001	0.176	0.0001	0.0001	0.159	0.035	0.0001	
N	164	164	164	164	164	164	164	164	164	164	

DISCUSSION

In this cross-sectional study, we identified significant correlations (p=0.01) between most risk factors and breast cancer, except for smoking, hormonal contraceptives, and age at menarche. The analysis of correlation coefficients between breast cancer risk and various risk factors reveals several noteworthy relationships (**Table III**). These correlations are critical in understanding the interplay between different risk factors and their collective impact on breast cancer incidence in this specific population.

The study identified significant positive correlations (at the 0.01 level) between breast cancer risk and most factors except smoking, oral contraceptive use, and age at menarche, which did not show a significant correlation. Specifically, age had the highest correlation coefficient with breast cancer risk ($r = .496$, $p < 0.0001$), indicating that increasing age is strongly associated with higher breast cancer risk. Family history also showed a notable correlation ($r = .363$, $p < 0.0001$), affirming the genetic predisposition to breast cancer. Family history is a well-established risk factor for breast cancer, yet 72% of the patients in this study lacked a family history, indicating that other non-genetic factors might play a more prominent role in this population.

Psychological stress had a significant correlation with breast cancer risk ($r = .373$, $p < 0.0001$), highlighting the role of chronic stress in increasing susceptibility to breast cancer. This finding aligns with the context of ongoing conflict and its impact on mental health, potentially exacerbating cancer risk. Body Mass Index (BMI) had a correlation coefficient of .355 ($p < 0.0001$), suggesting that higher BMI is significantly associated with increased breast cancer risk. The BMI data (**Table II**) showed a large proportion of patients with a BMI greater than 30 (45.1%), suggesting obesity is another significant risk factor. Obesity is known to increase the risk of breast cancer due to higher estrogen levels produced by adipose tissue. Recent studies have consistently shown that higher BMI is associated with an increased risk of developing breast cancer. For instance, a systematic review and meta-analysis of one hundred and two studies found that obese postmenopausal women have a 26% higher risk of breast cancer compared to their non-obese counterparts[25]. Furthermore, adipose tissue in obese individuals produces estrogen, which can stimulate the growth of estrogen receptor-positive breast cancer cells. Obesity-related metabolic disturbances, including insulin resistance and chronic inflammation, can contribute to cancer progression[26].

Breastfeeding showed a positive correlation ($r = .430$, $p < 0.0001$) (**Table III**), indicating its typical protective effect against breast cancer. However, the high prevalence of breastfeeding (78.7% for more than one year) (**Table II**) might not be providing the expected benefit due to severe and chronic war-related stress. Age at menarche had a lower correlation coefficient ($r = .106$) with no significant p-value ($p = 0.176$), indicating a weaker and statistically non-significant relationship with breast cancer risk. Age at menopause demonstrated a significant correlation ($r = .452$, $p < 0.0001$), suggesting that later age at menopause increases breast cancer risk due to prolonged estrogen exposure. The age at first birth, although correlated ($r = .290$, $p < 0.0001$), showed a less intense relationship than other factors. The reproductive history of the patients revealed that 45.2% had their first pregnancy before age 20, which is generally considered protective against breast cancer. However, the mild or high levels of psychological distress reported (71.4%) (table 2) could negate these protective factors.

Though no notable differences were found among the three age groups in breast cancer risk via the Kruskal–Wallis test, the occurrence at young ages hints at additional factors beyond the traditional ones for breast cancer. Our patients experienced breast cancer at notably young ages,

with the youngest patient being 24 – a comparatively early occurrence. In our study, the average age of breast cancer patients was 47.14, lower than neighbouring countries like the Gaza Strip (average 54.9, SD = 10.9), showing a nearly ten-year difference[27]. In Jordan, those under 40 comprised 15.6%, 40-49 years constituted 29.1%, and 50-59 years constituted 25.6% [28]. Our study had nearly double the cases under age 40 compared to Jordan, signaling an earlier onset in Syria than in neighbouring nations.

Breast cancer's causes vary globally. Our patients shared common breast cancer risk factors globally, yet in the Northwest region of Syria, there is notably a higher ratio of cases under age 40. Both patients under 40 and those aged 41-50 accounted for 32.9% of breast cancer diagnoses. In contrast, in Damascus and surrounding regime-controlled areas, patients aged 27-42 were 16.7%, and those aged 43-50 were 28.9% of breast cancer cases[29]. Damascus and surrounding Syria have better environmental conditions and have not suffered from continuous bombardment for the last decade; this might explain the doubled rate of women under 40 with breast cancer in Northwest Syria versus regime-controlled territories.

In war-hit Northwest Syria, additional breast cancer risks might exist amid ongoing chaos for 12 years, causing immense psychological pressure. Studies have highlighted the role of chronic stress in modulating the endocrine system, leading to an environment conducive to cancer development. Stress from prolonged conflict could significantly contribute as a risk factor for breast cancer[30]. A meta-analysis of several cohort studies has shown that previous experiences of stressful life events increase the risk of breast cancer[31-33]. Furthermore, studies suggest that when environmental risk factors occur along with conventional risk factors such as early age and genetic and hormonal influences, the effects may be additive and intensified[2]. One large cohort study of twins from Scandinavian countries (Finland, Denmark and Sweden) looked at data on 44,788 pairs of twins to assess the risks of cancer at 28 anatomical sites for the twins of persons with cancer. The findings of this study demonstrated that environmental factors such as stress are equally if not more important than genetic factors in causing cancer[34]. Likewise, it was shown that glucocorticoids, which are stress hormones, can enhance breast cancer metastasis by altering the tumor microenvironment[35]. These hormones influence cancer cell behavior, promoting invasion and dissemination, thus complicating the hormonal landscape and increasing the challenge of treating hormone-sensitive breast cancers; this shows the critical role played by stress in cancer progression.

CONCLUSION

In conclusion, our study in Northwest Syria, amidst over a decade of conflict, illuminates the critical issue of breast cancer prevalence. Focusing on ten risk factors among 164 biopsy-confirmed female breast cancer patients, we uncovered significant correlations, excluding smoking, age at menarche, and hormonal contraceptive use. Notably, our findings disclosed a substantial ten-year reduction in the average age of breast cancer onset, attributed to environmental factors ranging from chronic stress to continuous pollution from chemical bombing and remnants of war during this prolonged conflict – a key driver of earlier and increased incidents among Syria's younger female demographic. These insights highlight the urgency of addressing environmental concerns and implementing targeted interventions to mitigate conflict's impact on breast cancer incidence. Women in conflict zones face unique challenges, and our study advocates the need for further research in this area, aiming to fully understand the underlying causes of breast cancer and its early onset in Syria compared to neighbouring countries.

Ethics permission: Idlib University, Idlib, Syria, REC letter No. IUREC-20220101.
Informed consent was obtained from the patients. The Declaration of Helsinki maintained patient privacy and data confidentiality.
Conflict of interest: The authors declare no conflict of interest.
Financial disclosure: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.
Data Sharing Statement: The corresponding author can provide the data proving the findings of this study on request. Privacy or ethical restrictions bound us from sharing the data publicly.

AUTHOR'S CONTRIBUTIONS

Mutair YA: Major contribution to surgical procedures, data collection, data analysis and writing the manuscript
Mushtaq G: Major contribution to drafting and revising the work for important intellectual content.
Al-Daoud F: Major contribution in conceptualizing the study design, interpretation of results and supervision of the study
Al-Qassim M: Significant contribution in assisting in the surgical procedures and data collection
Hariri M: Significant contribution in conceptualizing the study design and supervision of the study

REFERENCES

1. Atassi B, Tse G, Mkhallalati H, Debel J, Jemmo A, Khalil M, et al. Cancer Diagnoses during Active Conflict: Experience from a Cancer Program in Northwest Syria. Avicenna J Med. 2022;12:157–61.
2. Xu H, Xu B. Breast cancer: Epidemiology, risk factors and screening. Chinese J Cancer Res. 2023; 35: 565-83.
3. Liu X, Yue J, Pervaiz R, Zhang H, Wang L. Association between fertility treatments and breast cancer risk in women with a family history or BRCA mutations: a systematic review and meta-analysis. Front Endocrinol (Lausanne). 2022; 13.
4. Davies L, Milner DA, Shulman LN, Kyokunda L, Bedada A, Vuylsteke P et al. Analysis of Cancer Research Projects in Sub-Saharan Africa: A Quantitative Perspective on Unmet Needs and Opportunities. JCO Glob Oncol. 2023;
5. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin. 2020;70:7–30.
6. Russo J, Moral R, Balogh GA, Mailo D, Russo IH. The protective role of pregnancy in breast cancer. Breast Cancer Res. 2005; 7: 131.
7. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50 302 women with breast cancer and 96 973 women without the disease. Lancet. 2002; 360: 187-95.
8. Alexeeff SE, Odo NU, McBride R, McGuire V, Achacoso N, Rothstein JH et al. Reproductive Factors and Mammographic Density: Associations Among 24,840 Women and Comparison of Studies Using Digitized Film-Screen Mammography and Full-Field Digital Mammography. Am J Epidemiol. 2019; 188: 1144–54.
9. Dall GV, Britt KL. Estrogen Effects on the Mammary Gland in Early and Late Life and Breast Cancer Risk. Front Oncol. 2017; 7: 110.
10. Arzanova E, Mayrovitz HN. The Epidemiology of Breast Cancer. In: Breast Cancer. Exon Publications; 2022. p. 1–20.
11. Chlebowski RT, Aragaki AK. The Women's Health Initiative randomized trials of menopausal hormone therapy and breast cancer: findings in context. Menopause. 2023; 30: 454-61.
12. Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and risk of breast cancer: nested case-control studies using the QResearch and CPRD databases. BMJ. 2020; m3873.
13. Kuchenbaecker KB, Hopper JL, Barnes DR, Phillips KA, Mooij TM, Roos-Blom MJ, et al. Risks of Breast, Ovarian, and Contralateral Breast Cancer for BRCA1 and BRCA2 Mutation Carriers. JAMA. 2017; 317: 2402.
14. Anisman H, Kusnecov AW. Cancer how lifestyles may impact disease development, progression and treatment. Academic Press; 2022.
15. Werts SJ, Robles-Morales R, Bea JW, Thomson CA. Characterization and efficacy of lifestyle behavior change interventions among adult rural cancer survivors: a systematic review. J Cancer Surviv. 2023;
16. Schwartz SM. Epidemiology of Cancer. Clin Chem. 2024; 70: 140-9.
17. Zeinomar N, Qin B, Amin S, Lin Y, Xu B, Chanumolu D et al. Association of Cigarette Smoking and Alcohol Consumption With Subsequent Mortality Among Black Breast Cancer Survivors in New Jersey. JAMA Netw Open. 2023; 6: e2252371.
18. Aburto TC, Romieu I, Stern MC, Barquera S, Corvalán C, Hallal PC et al. Latin American

and the Caribbean Code Against Cancer 1st edition: Weight, physical activity, diet, breastfeeding, and cancer. Cancer Epidemiol. 2023; 86: 102436.
19. Malcomson FC, Parra-Soto S, Ho FK, Lu L, Celis-Morales C, Sharp L et al. Adherence to the 2018 World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) Cancer Prevention Recommendations and risk of 14 lifestyle-related cancers in the UK Biobank prospective cohort study. BMC Med. 2023; 21: 407.
20. Brewer HR, Jones ME, Schoemaker MJ, Ashworth A, Swerdlow AJ. Family history and risk of breast cancer: an analysis accounting for family structure. Breast Cancer Res Treat. 2017; 165: 193-200.
21. Stanford JL, Herrinton LJ, Schwartz SM, Weiss NS. Breast cancer incidence in Asian migrants to the United States and their descendants. Epidemiology. 1995; 6: 181-3.
22. Ziegler RG, Hoover RN, Pike MC, Hildesheim A, Nomura AMY, West DW et al. Migration patterns and breast cancer risk in Asian-American women. JNCI J Natl Cancer Inst. 1993; 85: 1819-27.
23. Penberthy JK, Stewart AL, Centeno CF, Penberthy DR. Psychological Aspects of Breast Cancer. Psychiatr Clin North Am. 2023; 46: 551-70.
24. Armstrong K, Eisen A, Weber B. Assessing the Risk of Breast Cancer. N Engl J Med. 2000; 342: 564-71.
25. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023; 23: 392.
26. Agurs-Collins T, Ross SA, Dunn BK. The Many Faces of Obesity and Its Influence on Breast Cancer Risk. Front Oncol. 2019; 9.
27. El Sharif N, Khatib I. Reproductive factors and breast cancer risk in Palestine: A case-control study. Cancer Epidemiol. 2021; 74: 102019.
28. Abdel-Razeq H, Mansour A, Jaddan D. Breast cancer care in Jordan. JCO Glob Oncol. 2020; 6: 260-8.
29. Husein S, Hanafi I, Balouli M, Baradi Z, Alsheikhah Y, Abo Samra D, et al. Breast cancer screening during the Syrian crisis: A cross-sectional study. J Prev Med Hyg. 2021; 62: E520-8.
30. Bowen DJ, Fernandez Poole S, White M, Lyn R, Flores DA, Haile HG, et al. The role of stress in breast cancer incidence: risk factors, interventions, and directions for the future. Int J Environ Res Public Health. 2021; 18: 1871.
31. Barnard ME, Wang X, Petrick JL, Zirpoli GR, Jones D, Johnson WE, et al. Psychosocial stressors and breast cancer gene expression in the Black Women's Health Study. Breast Cancer Res Treat. 2023;
32. Bahri N, Fathi Najafi T, Homaei Shandiz F, Tohidinik HR, Khajavi A. The relation between stressful life events and breast cancer: a systematic review and meta-analysis of cohort studies. Breast Cancer Res Treat. 2019; 176: 53-61.
33. Pereira MA, Araújo A, Simões M, Costa C. Influence of Psychological Factors in Breast and Lung Cancer Risk – A Systematic Review. Front Psychol. 2022; 12.
34. Lichtenstein P, Holm N V, Verkasalo PK, Iliadou A, Kaprio J, Koskenvuo M et al. Environmental and heritable factors in the causation of cancer—analyses of cohorts of twins from Sweden, Denmark, and Finland. N Engl J Med. 2000; 343: 78-85.
35. Obradović MMS, Hamelin B, Manevski N, Couto JP, Sethi A, Coissieux MM et al. Glucocorticoids promote breast cancer metastasis. Nature [Internet]. 2019; 567: 540-4.