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Original Article

A study of risk factors for breast cancer in Al-Anbar province: a case-control study

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Abstract

Background: Globally, breast cancer is a widespread malignancy among women, ranking as the second leading cause of female mortality. This study investigates risk factors for breast cancer in AL-Anbar province, Iraq, emphasizing their significance in disease development.

Methods: An investigation was carried out at Al-Anbar Cancer Center in Al-Anbar province, Iraq, employing a case-control design. The study comprised 60 confirmed breast cancer cases and 120 controls without breast issues. Data was collected through direct interviews using a semi-structured questionnaire, and subsequent analyses included descriptive, bivariate, and multivariate approaches.

Results: About 48.0% aged 41-49, and 25% aged 50-59. Case and control groups were matched in age, but varied in marital, education, occupation, menopausal status. Women with benign breast diseases have a 1.7 times higher breast cancer risk (OR=1.7, CI=0.063-4.53). Positive family history triples the risk (OR=3, CI=1.21-7.80, P=0.002), and the sedentary lifestyle exhibits 5 times higher risk of breast cancer (OR=5.67, CI=2.89-4.13, P < 0.001). Menstrual age, parity, and reproductive factors influence breast cancer risk. Menarche at ≤12 years triples the risk (OR=3.05, CI=1.82-5.05, P<0.001), while menarche at ≥16 decreases it (OR=0.89, CI=0.06-5.12, P<0.001). Nulliparity increases risk 2.1 times (OR=2.1, CI=0.8-4.89, P=0.002), and more live births provide significant protection. Preterm delivery before the eighth month triples the risk (OR=2.9, CI=1.32-6.53, P=0.002). Multiple children prevent breast cancer, while mother's age at first full birth ≥30 raises the risk 3.5 times (OR=3.4, CI=1.45-7.88, P=0.014). Women who never breastfed had a significant twofold higher risk of breast cancer (OR=2, CI=0.8-4.38, P=0.003). Postmenopausal women at ≥50 years faced a threefold higher risk than their counterparts (OR=3.25, CI=1-1.11, P=0.004). Hormonal use showed a marginal risk increase (OR=1.2, CI=0.5-1.8, P<0.001).

Conclusion: Breast cancer susceptibility arises from diverse factors like genetics, nutrition, environment, and lifestyle. Effectively managing and preventing breast cancer involves implementing strategic control measures.

Keywords: Breast Cancer, Risk Factors, Anbar Cancer Center, Menopausal Status, Family History, Menstrual Status, Body Weight, Iraq

Background

Globally, breast cancer stands as a prevalent malignancy in women, ranking second in female mortality. It accounts for 15% of all female cancer deaths and constitutes 26% of newly diagnosed cancers in women, as reported in 2008 [1]. The worldwide burden escalated with approximately 1.5 million new cases diagnosed in 2004. In England and Wales, one in twelve women is projected to face this illness at some point [2]. Globally, breast cancer poses a substantial concern. It ranks as the most prevalent cancer in women, with approximately 2.1 million new cases annually, comprising 24.2% of all female cancer diagnoses and contributing to 15% of mortality [3]. Breast cancer is a complex condition without a singular etiology, characterized by various risk factors. Epidemiological studies have identified elements such as gender, age, family history, and race as contributors to its development. Females, due to hormonal influences, particularly estrogen and progesterone, face a higher risk compared to males, as these hormones prompt accelerated growth and changes in breast cells. Advancing age, with women over 30 being notably vulnerable, adds to the risk profile. While screening mammography is a common practice, its application in females under 50 remains debated due to higher false-positive results and challenges associated with dense breast tissue [4]. Furthermore, younger women exhibit a lower

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likelihood of developing breast cancer, reducing the effectiveness of mammography in early detection. Despite this, population-wide benefits of screening mammography for those aged 40 to 49 appear to outweigh the risks. Regular mammography in women over 50 contributes to a 35% reduction in breast cancer mortality, proving a safe and cost-effective measure. Various risk factors, such as high socioeconomic status, early pregnancy age, mammographic changes, benign proliferative lesions, cancer history in one breast, and family history, influence relative risks. Conversely, low-risk factors include null parity, postmenopausal obesity, and a high-fat diet. Urban residence, Black race (below 45 years), older age irrespective of race, and a history of endometrial or ovarian cancer are associated with elevated risks [5,6]. Examining breast cancer risk factors is pivotal, influencing critical medical decisions for women. These factors impact choices such as initiating postmenopausal hormone replacement therapy, commencing mammogram screening, using tamoxifen for prevention, or opting for preventive mastectomy. Postmenopausal hormone replacement therapy has gained widespread use for alleviating estrogen deficiency symptoms, including hot flashes, night sweats, osteoporosis, and cognitive impairment [7,8]. Current recommendations issued by American Cancer Society advise women with a genetic predisposition to breast cancer to undergo a baseline mammogram at 35, initiating annual screenings at 40 [9]. A common indicator of breast cancer is a palpable lump in the breast. However, a significant number of women presenting with breast concerns may lack apparent external signs of breast disease [10]. Additionally, breast pain (mastodynia) or a painful lump can signal early breast cancer. In some cases, breast cancer manifests as metastatic, spreading beyond the initial organ, with symptoms depending on the affected areas like bone, liver, lung, or brain [11]. Low-income regions like Sub-Saharan Africa and Asia exhibit a lower risk of breast cancer [12]. While Western nations see a rising incidence, mortality remains stable or decreases due to early detection and improved treatments. Breast cancer, most prevalent in both Middle Eastern and Western women, is influenced by societal trends like delayed marriages and limited childbirth in the West. Preventative measures include breastfeeding and lifestyle adjustments to reduce postmenopausal occurrences [13]. In Iraq, breast cancer is the predominant tumor type among women over 40, with incidence tripling in the last decade [14,15]. The most recent Iraqi Cancer Registry, breast cancer makes up about one-third of all recorded female cancers [16]. According to the 2018 World Health Organization report, breast cancer in Iraq ranked prominently, with an incidence rate of 20.3% and a mortality rate of 11.9% [17]. This study aimed to detect breast cancer risk factors among Iraqi women living in Al-Anbar province.

Methods

Study design

A case control study was conducted from February 2023 throw July 2023 at Al-Anbar Cancer Center in AL-Anbar province, west of Iraq.

Inclusion and exclusion criteria

The case group comprised Iraqi females diagnosed with breast cancer, aged 18 and above, stable, conscious, and willing participants. The control group involved volunteers, clinically and self-assessed as healthy females, aged 18 and above, or willing patients' relatives. The study excluded other types of cancer, severely ill patients, aged less than 18 years and those unwilling to participate.

Samples Size

As per WHO data (2020) [18], Iraq has approximately 79,000 cancer patients. The study required a minimum sample of 188 with 90% confidence, 0.5 standard deviation, and a 6% margin of error.

Sampling procedure

The study employed convenience sampling technique to invite cancer patients receiving standard care at the oncology cancer center to participate. Eligible patients, identified through clinic receptionists during chemotherapy visits, were interviewed (face-to-face) by the two researchers. After explaining the study's aims, Arabic-language consent forms and information sheets were provided. Participants were informed that their agreement to participate and share information served as written consent. This approach facilitated recruitment and ensured clarity on participation expectations in the study.

Study tool

A semi-structured questionnaire, divided into four sections, was used to collect data. Patient medical files provided some information. The first section covered sociodemographic variables (age, marital status, education, occupation, menopausal status, residence). The second focused on risk factors (benign breast disease history, family history of breast cancer, body mass index, physical activities). The third included reproductive risk factors (menstrual age, parity, live births, stillbirths, preterm delivery, miscarriage, multiple births, mother's age at first full birth, breastfeeding, hormonal contraceptive use). This comprehensive approach aimed to gather diverse information for a holistic analysis.

Statistics analysis

SPSS software, version 16, was utilized for data analysis. Discrete variables were expressed as frequency and percentage. Odds ratios with a 95% confidence interval ($P < 0.05$) indicated statistical significance. A significance level of 5.0% was set. Logistic regression identified variables associated with case and control groups, providing a comprehensive statistical approach for result interpretation.

Results

Table 1 reveals comparable age distribution between case and control groups, with around 48.0% aged 41-49, 25.0% aged 50-59 years, 17.0% below 40 years, and 10.0% were 60 years or older. Marital status showed 78.0% married in the case group, 73.0% in the control group, and 22.0% unmarried in the case group, 27.0% in the control group. Education levels differed, with 48.0% illiterate in the case group, 28.0% in the control group, and variations in primary, secondary, and higher education. Occupation-wise, 67.0% of the case group were housewives, compared to 54.0% in the control group, and 18.0% of the case group were employees, versus 25.0% in the control group. Menopausal status varied, with 75.0% pre-menopausal and 25.0% post-menopausal in the case group, while the control

group had 60.0% pre-menopausal and 40.0% post-menopausal, with corresponding age-of-menopause distinctions. Residential distribution was 59.0% urban and 41.0% rural in the case group, versus 71.0% urban and 29.0% rural in the control group.

Table 1: Distribution of subjects according to menopausal status and socio-demographic characteristics (n=180)

Variables	Categorization	Case		Control	
		No.	%	No.	%
Age	≤ 40	10	17	19	16
	41-49	29	48	59	49
	50-59	15	25	29	24
	≥ 60	6	10	13	11
Marital status	married	47	78	88	73
	Single	13	22	32	27
Education of women	Illiterate	29	48	34	28
	Read &write	3	5	12	10
	Primary	17	28	19	16
	Secondary	7	12	30	25
	University &above	4	7	25	21
Women occupation	House wife	40	67	65	54
	Employed	11	18	30	25
	Not employed	9	15	25	21
Menopausal status	Pre-menopausal	45	75	72	60
	Post-menopausal	15	25	48	40
Age at menopause Cases=14	50>	4	28	36	75
Controls=48	50≤	10	72	12	25
Residence	Rural	25	41	35	29
	Urban	35	59	85	71

In Table 2, women with a history of benign breast diseases exhibited a 1.7 times higher risk of breast cancer (OR=1.7, CI=0.063-4.53). A positive family history significantly increased breast cancer risk by three times compared to those without such history (OR=3, CI=1.21-7.80, P=0.002). Overweight and obese women (BMI ≥ 25 Kg/m²) showed no significant risk (OR=1.2, CI=0.49-5.52, P=0.66). In terms of exercise, those with a sedentary lifestyle faced a 5 times higher risk of breast cancer (OR=5.67, CI=2.89-4.13, P < 0.001), while moderate exercise correlated with a lower risk. Positive family history and sedentary lifestyle emerged as potential contributors to breast cancer development.

Table 2: Distribution of subjects according to risky factors of breast cancer (n=180)

Risk factors	Categorization	Case		Control		OR	95% C. I	P Value
		No.	%	No.	%			
History of benign breast diseases	Yes	8	13	10	8.3	1.7	0.63—4.53	0.27
	NO	52	87	110	91.7	k		
Family history of breast cancer	yes	12	20	9	7.5	3	1.21—7.80*	0.002
	No	48	80	111	92.5	k	k	
Body mass index	< 25	11	18	20	17	1.12	0.49—2.52	0.66
	≥ 25	49	82	100	83		k	
History of physical activities	Mild	38	63	28	23	5.67	2.89—11.13*	<0.001
	Moderate	22	37	83	69			
	Sever	0	0	9	8			

Table 3 displays menstrual age and reproductive factors in relation to breast cancer risk. For cases, 50.0% had menarche at 13-15 years, with 48.0% at ≤ 12 and 2.0% at ≥ 16. Controls had 74.0% at 13-15, 23.0% at ≤ 12, and 3.0% at ≥ 16. Menstrual age ≤ 12 increased breast cancer risk by threefold (OR=3.05, CI=1.82-5.05, P<0.001), while menarche at ≥ 16 decreased risk (OR=0.89, CI=0.06-5.12, P<0.001). Nulliparity increased breast cancer risk 2.1 times (OR=2.1, CI=0.8-4.89, P=0.002). More live births significantly protected against breast cancer (OR=0.8 for 1-3 births, 0.4 for 4-6, and 0.4 for 7+ vs. nulliparous, P=0.002). No change in risk was observed for women with a history of one or more stillbirths (OR=1, CI=0.04-5.57, P=1.0). Preterm delivery before the eighth month increased risk threefold (OR=2.9, CI=1.32-6.53, P=0.002), while no risk was observed after eight months (OR=0.8, CI=0.2-3.1). One miscarriage had no risk (OR=0.80, CI=0.34-1.86), while multiple miscarriages showed a slight increase (OR=1.17, CI=0.56-2.43, P=0.57). Multiple children prevented breast cancer (OR=0.32, CI=0.12-0.86, P=0.019). Mother's age at first full birth ≥ 30 increased risk 3.5 times (OR=3.4, CI=1.45-7.88, P=0.014), while ages 21-29 had a slight effect (OR=1.4, CI=0.77-2.42).

Table 3: Distribution of subjects according to reproductive risk factors and birth outcomes for breast cancer (n=180).

Risk factors	Categorization	k	Case	Control	Control	OR	95% C.I	P value
		No.	%	No.	%	k	k	k
Menstrual age (years)	≤ 12	29	48	28	23	3.05	1.82-5.05*	k
	13-15	30	50	89	74	k	k	<0.001
	≥ 16	1	2	3	3	0.89	0.06-5.12	k
Parity	nulliparous	11	18	12	10	2.1	0.8-4.89*	0.02
	parous	49	82	108	90			
No. of live births	absent	11	18	12				0.002
	1-3	25	42	34		0.80	0.30-2.11	
	4-6	13	21	33		0.4	0.15-1.21*	
	≥ 7	11	19	41		0.4	0.20-0.7*	
Previous history of stillbirths	0	59	98	118	98	1.0	0.04-5.57	1.0
	≥ 1	1	2	2	2			
Previous history of preterm delivery	0	40	67	97	81			0.002
	<8 months	17	33	14	11	2.94	1.32-6.53*	k
	≥8	3	5	9	8	0.8	0.2-3.1	k
Previous history of miscarriage	never	33	55	66	55	k		0.57
	one	10	17	25	21	0.80	0.34-1.86	k
	More than one	17	28	29	24	1.17	0.56-2.43	k
History of multiple birth	yes	3	5	17	14	0.32	0.12-0.86*	0.019
	no	57	95	103	86			
Mother's age at first full birth (years) Cases =49; Control=108	≤20	18	37	56	52			0.014
	21-29	20	41	42	39	1.4	0.77-2.42	
	≥30	11	22	10	9	3.4	1.45-7.88*	

In Table 4, women who never breastfed (23%) were at a significant 2 times higher risk of breast cancer than those who breastfed (OR=2, CI=0.8-4.38, P=0.003). Postmenopausal women at ≥ 50 years had a threefold higher risk compared to those reaching menopause at < 50 years (OR=3.25, CI=1-1.11, P=0.004). Hormonal use, with 62% in both cases and controls having never used it, showed a marginal risk increase (OR=1.2, CI=0.5-1.8, P<0.001) when compared to non-users. The results underscore the impact of breastfeeding, menopausal age, and hormonal use on breast cancer risk.

Table 4: Distribution of subjects according to breast feeding, menopausal status, and uses of hormonal contraceptive for breast cancer (n=180)

Risk factors	Categorization	Case		Control		OR	95% C. I	P Value
		No.	%	No.	%			
Breast feeding	No breast feeding	14	23	16	13			
	Breast feeding	46	77	104	87	2	0.8-4.38*	0.003
Age at menopause (year) Cases=14	< 50	4	29	29	59	k	k	k
Controls=49	≥ 50	10	71	20	41	3.25	1-11.1*	0.004
Hormonal contraceptive use	Never	37	62	74	62	k	k	k
	Current use	0	0	6	5	1.13	0.36-3.51	<0.001
	Previous use	23	38	40	33	1.2	0.5-1.8	k

Discussion

This study indicates that breast cancer is most prevalent among women aged 40-49 (48%), followed by those aged 50-59 (25%), and only 10% in the ≥60 age group. The findings align with previous research in Iraq and Qatar [19,20,21], where the highest incidence was observed in the 40-49 age range. However, contrasting results were noted in Europe, where only 25% of cases were >50 years old [22]. This suggests age distribution patterns in breast cancer may vary across regions, influencing screening and intervention strategies. Moreover, Rahou 's study [23] aligns with ours, revealing breast cancer is more prevalent in women under 50 in Iraq, Jordan, Lebanon, Tunisia, and Kuwait. In contrast, a U.S. study, influenced by a different population pyramid and higher life expectancy, found breast cancer more common in women aged 50 and older. Our findings reveal that 78.0% of breast cancer cases were married, in line with Alwan's report on Iraqi women [15]. The impact of education level on breast cancer risk is debated; our study suggests a 35.0% reduced risk with higher education, contrary to Dong and Qin 's findings [24]. This contrasts with Liu's study showing no association [25]. Our results align with Mukama et al.'s study, indicating a higher percentage of cases in the illiterate group [26]. These diverse findings emphasize the complexity of the relationship between marital status, education, and breast cancer risk across different populations. The current study found that 75.0% of cases were premenopausal, aligning with Mammographic breast density, its changes, and breast cancer risk in premenopausal and postmenopausal women et al.'s research

[27], linking the rising breast cancer incidence to a notable effect on premenopausal women. Additionally, 59.0% of cases were from urban areas, similar to Abdel hakiem et al.'s findings in Egypt, where breast cancer frequency was notably higher in metropolitan areas [28]. In terms of benign breast cancer history, 13.0% of cases had it, compared to 8.3% in the control group, though without significant association. Despite the lack of association, certain types of benign breast cancers are still linked to breast cancer risk, with the highest risk associated with proliferative lesions with atypia [29]. Similar to previous finding reported by Mukama et al. [30], positive family history emerged as a significant risk factor, with 20.0% of cases and 80.0% of controls having such history, showing a threefold increased risk. This study indicates that a body mass index (BMI) ≥25 Kg/m is associated with reduced breast cancer risk (OR=0.88, P=0.66), potentially linked to chemotherapy-induced weight loss. Furthermore, the findings support the association between physical exercise and breast cancer risk, revealing a 5.67 times higher risk for mild versus moderate physical activity (p<0.001). Regular exercise may contribute to breast cancer prevention through hormonal influences on estrogen and progesterone levels [31]. The current study highlights early menarche as a significant risk factor, with a 3.05 times higher risk for breast cancer in those with menarche at age ≤12 compared to those at 13-15 years, consistent with prior research linked early menarche to higher estrogen levels [32,33]. Nulliparity is linked to a two-fold increased risk compared to parous patients (p=0.02), aligning with existing studies emphasizing the higher risk for nulliparous women [34]. Unmarried women aged 40-54 face a 4-5 times higher risk of breast cancer compared to married counterparts, as indicated by a study in India [35]. Additionally, the study underscores a protective effect with a higher number of live births (OR=0.8, CI=0.30-2.11), and a significant risk reduction for women with 7 or more births (OR=0.4, CI=0.20-0.65, P=0.002). These findings echo studies emphasizing the protective role of multiple full-term pregnancies against breast cancer [36]. In this study, a history of stillbirths demonstrated no correlation with an increased risk of breast cancer (OR=1.0, P=1.0), echoing findings from another study [37]. Regarding preterm delivery, there was a significant 2.94 times higher breast cancer risk for patients with preterm delivery before the eighth month of gestation (OR=2.98, P=0.002). However, preterm delivery at ≥8 months showed no heightened risk (OR=0.8), suggesting a protective effect beyond 8 months, aligning with similar findings [38]. Miscarriage exhibited no association with breast cancer risk in the current study (P=0.57), consistent with prior research [39]. Patients with a history of multiple births did not display a significant decrease in breast cancer risk (OR=0.32, P=0.019). Despite this, a study suggested an increased risk of breast cancer following twin pregnancies due to elevated gonadotropin levels [40]. The study unveiled those women with a first full-term delivery at ≥30 years faced a 3.4 times higher risk than those ≤20 years (OR=3.4, P=0.14). Similarly, those with a first full-term delivery at 21-29 years showed an increased risk (OR=1.4, P=0.14), consistent with research indicating a 5.4 times greater relative risk for women having their first child beyond 30 years compared to 15 years after their first delivery [41]. Concerning breastfeeding, this study reveals a two-fold decrease in breast cancer risk among breastfeeding women (p=0.003), aligning with findings in other studies [42,43]. Developed countries' research emphasizes the protective impact of breastfeeding duration against breast cancer [44]. The study highlights a significant increase in breast cancer risk for women ≥50 years old compared to those with menopause at age <50 (OR=3.25, P=0.004), in concordance with similar findings mentioned in the world cancer report on 2020 [45]. Older menopausal women face heightened breast cancer risk due to prolonged exposure to estrogen and progesterone, supported by studies like Kelsey et al.'s [46], linking late menopause to increased breast cancer risk. Women with a history of oral contraceptive use show a mild increase in breast cancer risk (OR=1.2, P=<0.001), in agreement with a health study cohort [47] indicating a mild elevation in breast cancer risk among females aged 24-43 using oral contraceptives. The case-control design is susceptible to biases such as selection, non-response, and information bias. However, this study mitigated selection bias by identifying cases through histopathology at Al-Anbar Cancer Center. The questionnaire's simplicity aimed to minimize information bias. All cases visiting the center, whether for the first time or follow-up, were included during researchers' weekly visits. Repeated visits were excluded. Approximately 10% non-response cases were excluded due to chemotherapy-induced fatigue. The study acknowledges wide confidence intervals owing to its small sample size.

Conclusion

Breast cancer peaks between ages 40 and 49, with early menarche (<12 years) linked to a threefold higher risk than menarche at 13–15 years. Woman having her first full-term birth at 30 faces about 3.5 times higher breast cancer risk than those at 20. Increased parity provides significant protection, with nulliparous women having twice the risk of breast cancer. Preterm delivery before 8 months raises breast cancer risk threefold, while beyond 8 months poses no risk. Multiple births reduce breast cancer risk, and women reaching menopause at ≥50 face a 71% breast cancer risk. Late menopause increases breast cancer risk. Positive family history, obesity, and previous hormonal use also elevate breast cancer risk. Researchers advocate family planning program visits for advice on marriage age, first birth age, child spacing, and encouraging higher parity.

Abbreviation

OR: Odds Ratio; CI: Confidence Interval; BMI: Body Mass Index; WHO: World Health Organization

Declaration

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Availability of data and materials

Data will be available by med.yaseen.anbar@uoanbar.edu.iq

Authors' contributions

Yaseen T. Sarhan (YTS), and Raghda Bardan (RB) are equally conceived and designed the questionnaire; distributed the questionnaire; analyzed and interpreted the data; drafted the manuscript; revised the manuscript. All authors have read, reviewed, and approved the final manuscript.

Ethics approval and consent to participate

We conducted the research following the declaration of Helsinki. The study protocol was approved by the scientific research ethics committee at college of medicine, University of Anbar (No: 66 on 20th December 2022). Informed consent was obtained from the participants before filling out the survey questionnaire.

Consent for publication

Not applicable

Competing interest

The authors declare that they have no competing interests.

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