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Factors Increasing the Risk of Breast Cancer in Libyan Women

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A B S T R A C T

Libyan breast cancer research is limited. Thus, it is crucial to look into the risk factors for breast cancer in Libyan women, as this could improve our current knowledge of this significant problem. Recent years have seen an increase in the disease's incidence among women both globally and in Libya, with Libyan women receiving diagnoses earlier. As a result, it is crucial to identify the factors that may be contributing to this increase. This study aims to investigate and analyze different factors linked to an increased risk of breast cancer in Libyan women. This case-control study involved 102 Libyan women, conducted at the National Institute for Cancer Therapy in Gharian and Tripoli University Hospital in Tripoli, Libya. Participants were divided into two groups: 51 diagnosed with breast cancer matched with 51 healthy controls, and both groups completed a face-to-face questionnaire. Inclusion criteria: Libyan females with breast cancer at age 18 >. Exclusion criteria: males and any nationality other than Libyan. The study investigated risk factors associated with breast cancer among Libyan women using SPSS (27). Clinical results showed that most diagnoses were at stage II, and that left-sided cancers were more common. Metastasis was present in one-third of the patients. Breastfeeding habits, parity, body mass index (BMI), sociodemographic factors (education, marital status, and socioeconomic status), and reproductive and menopausal characteristics (age at menarche, age at first pregnancy, and menopausal status) did not show a significant correlation with the risk of breast cancer. Conversely, factors were significantly associated with increased breast cancer risk. Age showed a strong relationship, with incidence rising in women aged 40 years and above. Vitamin D insufficiency or deficiency was common among patients and significantly associated with breast cancer occurrence. Metabolic disorders also played an important role, as diabetes (20.4% vs. 4.0% of controls) and hypertension (18.0% vs. 2.0% of controls) were significantly linked to higher risk. Hormonal factors were particularly notable, with both hormonal replacement therapy (37.3% vs. 2.0%) and oral contraceptive pill use (14.0% vs. 2.1%) associated with breast cancer. Additionally, women without a history of oophorectomy or hysterectomy were at higher risk, suggesting a protective effect of these procedures. Finally, family history was a significant predictor, appearing in 21.6% of cases compared to 3.9% of controls. This study showed that no significant link exists between reproductive, menopausal, sociodemographic, or lifestyle factors and breast cancer risk, but identified age (over 40), vitamin D insufficiency, diabetes, hypertension, hormonal therapy, oral contraceptive use, absence of oophorectomy or hysterectomy, and family history as strongly associated with breast cancer risk.

Introduction

Cancer represents a major global health burden, with incidence and mortality rates continuing to rise. The incidence of breast cancer has also significantly increased worldwide; in 2020, there were nearly 685,000 reported deaths and 2.3 million new cases. According to estimates, the age-standardized incidence rate is 18.8 per 100,000 women per year [1]. With 20–33% of female cancers and roughly 23% of all cancer cases nationwide, breast cancer is the most prevalent cancer among women in Libya. Libyan women are frequently diagnosed with more advanced disease stages and at younger ages than women in industrialized nations [2].

Breast cancer is a complex disease that is impacted by many risk factors, though the development of the disease is not always caused by their presence. One of the most significant risk factors for breast cancer is age. Although postmenopausal women are most likely to experience the disease, younger women's cases are typically more aggressive and linked to worse outcomes. Studies show that the average age at presentation varies by region, with an average of 48 years in Africa and a later onset in Europe [3]. Hormonal factors also play a significant role. In addition to causing breast enlargement and tenderness, the use of oral contraceptive pills can overstimulate epithelial tissue and cause cancer because they act on estrogen-sensitive breast tissue [4]. Similarly, there is evidence that hormone replacement therapy (HRT) increases

the risk of breast cancer by 2% for every year of use [5,6]. The risk is further increased by genetic predisposition, since the lifetime risk is doubled if a first-degree relative has the disease before the age of 50. However, because of BRCA1/2 mutations, the risk can increase up to 14 times if both a mother and a sister are affected [4,7]. Furthermore, the risk of developing breast cancer is four to five times higher for women with benign breast disease, especially atypical hyperplasia like complex fibroadenomas, duct papillomas, or sclerosing adenosis, and the risk of recurrence is two to six times higher for those with a history of breast cancer [4].

The risk of breast cancer is also influenced by lifestyle factors. Increased incidence and a poorer prognosis have been linked to type 2 diabetes mellitus, which may be caused by insulin resistance and high blood glucose levels that supply too much energy for the growth of cancerous cells [8]. Although both conditions pose serious health risks, particularly for post-menopausal women, the connection between hypertension and breast cancer is still unclear [9, 10]. Vitamin D deficiency has also been linked because, through the vitamin D receptor (VDR), vitamin D regulates angiogenesis, differentiation, apoptosis, and cell proliferation in addition to maintaining calcium homeostasis. These defense mechanisms are compromised by low levels, which may aid in the development of cancer [11]. Collectively, these risk factors demonstrate how age, hormones, genetics, comorbidities, and lifestyle all interact intricately to shape the risk of breast cancer.

Methods

This case-control study was conducted among 102 Libyan women at Tripoli University Hospital (TUH), Tripoli, and the National Institute for Cancer Therapy in Gharian, Libya. Ethical approval was obtained orally from both institutions and from all participants. The study population was divided into two groups: 51 women with confirmed diagnoses of breast cancer and 51 healthy controls. Inclusion criteria were Libyan females over 18 years of age diagnosed with breast cancer at any stage, while exclusion criteria included males, non-Libyan nationals, patients with psychiatric disorders, and pregnant women. Data on descriptive characteristics and breast cancer risk factors were collected through face-to-face questionnaires. In addition, 5 mL blood samples were drawn from each participant to measure serum vitamin D levels. Laboratory analysis was performed at Alnhda Laboratory using the Ichroma™ Vitamin D Neo, a fluorescence immunoassay (FIA) for the quantitative determination of total 25-hydroxyvitamin D.

Data analysis was carried out using the Statistical Package for the Social Sciences (SPSS, version 27). Descriptive statistics, including frequencies and percentages, were used to summarize categorical variables. The chi-square (x^2) test of independence was applied to assess associations between breast cancer status and categorical risk factors. A p-value threshold was set to determine statistical significance for all analyses.

Results

According to the Materials and Methods, this study was conducted on 102 Libyan women, including 51 with confirmed breast cancer and 51 healthy controls, to investigate and analyse various factors potentially associated with an increased risk of breast cancer.

The analysis demonstrated that several factors were not significantly associated with breast cancer risk among Libyan women. Specifically, reproductive and menopausal characteristics such as age at menarche, age at first pregnancy, and menopausal status (pre- vs post-menopausal) did not differ significantly between cases and controls. Although breast cancer cases appeared slightly more frequent among women aged 35–50, this same pattern was also observed among controls, and therefore, it indicated no meaningful association. Similarly, sociodemographic variables, including marital status, socioeconomic level, and educational attainment, showed no significant differences between groups, and breastfeeding practices, together with parity status, were also comparable. In fact, most women in both groups had a history of childbirth, but there was no statistically significant relationship to breast cancer risk.

In contrast, clinical findings did reveal several important patterns among breast cancer patients. The predominant presentation was a palpable breast mass (47.1%), whereas cystic lesions (13.7%) represented the second most common finding. This trend aligns with international reports, since breast masses are generally the most frequent presenting symptom [12]. Moreover, left-sided breast cancer was observed more often than right-sided disease, and most women were diagnosed at stage II (29.4%), while stage III (11.8%) and stage IV (5.9%) followed. Furthermore, nearly one-third of patients (29.8%) presented with metastasis, which highlights not only the burden of advanced disease but also the critical importance of early detection. Although body mass index (BMI) was not statistically associated with breast cancer risk, both overweight and obesity were highly prevalent in cases as well as controls; thus, further research is warranted to clarify their potential contribution to disease burden.

Overall, the p-values from this study confirmed that there were no significant associations between the examined factors and breast cancer risk in this sample. Consequently, reproductive and menopausal

characteristics, together with sociodemographic and lifestyle variables, were not found to be significantly related to the development of breast cancer among Libyan women.

The distribution of breast cancer cases by age revealed that the majority of Libyan women were diagnosed between 35 and 50 years (58.8%), followed by 23.5% diagnosed after the age of 50, and 17.6% diagnosed before 35 years. Consequently, statistical analysis confirmed a highly significant difference across age groups (x^2 = 15.176, p < 0.001), thereby highlighting mid-life women as the most vulnerable group.

Furthermore, the analysis of age distribution reinforced the strong association between age and breast cancer occurrence (x^2 = 24.190, p < 0.001). While younger women under 40 years were more common in the control group (60.4% vs. 15.7% of cases), breast cancer cases were increasingly concentrated in older age groups. For instance, women aged 40–49 accounted for 31.4% of cases compared to 25.0% of controls, those aged 50–59 represented 29.4% of cases versus 8.3% of controls, and women over 60 made up 23.5% of cases versus only 6.3% of controls. Thus, these findings clearly indicate that breast cancer incidence rises significantly with advancing age among Libyan women (Table 1).

Table 1. Age-Specific Distribution of Breast Cancer Cases and Healthy Controls among Libyan Women with Corresponding Chi-Square Analysis and Statistical Significance

Age	Breast Cancer Case		Control		Chi square	P value
	Count	%	Count	%		
< 40	8	15.7	31	60.4	24.190	< 0.001
40-49	16	31.4	13	25.0		
50-59	15	29.4	4	8.3		
> 60	12	23.5	3	6.3		

In addition, serum vitamin D levels were significantly associated with breast cancer risk. Most breast cancer patients (76.5%) had insufficient vitamin D levels (10–30 ng/mL), whereas 13.7% were deficient (<10 ng/mL). In contrast, vitamin D deficiency was more frequent among controls (33.3%), while sufficient levels (>30 ng/mL) were observed slightly more often in breast cancer cases (9.8%) than in controls (3.9%). Accordingly, the chi-square test demonstrated a significant association between vitamin D status and breast cancer (x^2 = 6.143, p = 0.046), suggesting that altered vitamin D levels may contribute to disease risk in this population (Table 2).

Table 2. Comparison of Serum Vitamin D Status Between Breast Cancer Patients and Controls in Libya, Including Chi-Square Test Results and P-value

Vitamin D	Breast Cancer Case		Control		Chi square	P value
	Count	%	Count	%		
<10 ng\ml	7	13.7	17	33.3	6.143	0.046
10-30 ng\ml	39	76.5	32	62.7		
> 30 ng\ml	5	9.8	2	3.9		

Moreover, metabolic disorders were also significantly linked to breast cancer risk. Diabetes mellitus (DM) was present in 20.4% of breast cancer patients compared to 4.0% of controls (x^2 = 6.255, p = 0.012) (Table 3), while hypertension was observed in 18.0% of patients versus 2.0% of controls (x^2 = 7.281, p = 0.007). Therefore, women with diabetes or hypertension were proportionally more likely to develop breast cancer than those without these conditions, thereby underscoring the importance of metabolic health as a potential risk factor. Collectively, these results emphasize the need to address diabetes and hypertension as part of comprehensive breast cancer prevention and control strategies in Libyan women (Table 3).

Table 3. Prevalence of Diabetes Mellitus among Breast Cancer Patients and Healthy Controls in Libya with Chi-Square Analysis and Statistical Significance

Diabetes Mellitus	Breast Cancer Case		Control		Chi square	P value
	Count	%	Count	%		
Yes	10	20.4	2	4.0	6.255	0.012
No	41	79.6	49	96.0		

Similarly, hormonal factors were found to play a significant role in breast cancer risk. Hormone replacement therapy (HRT) use was reported by 37.3% of breast cancer patients compared to just 2.0% of controls, and statistical analysis confirmed a strong association (x^2 = 19.760, p < 0.001) (Table 4). Likewise, oral contraceptive pill (OCP) use was more common among breast cancer patients (14.0%) than controls (2.1%), with the difference being statistically significant (x^2 = 4.639, p = 0.031). These findings suggest that both

HRT and OCP use are associated with increased breast cancer risk, thereby underscoring the influence of hormonal exposure on disease development (Table 4).

Table 4. Use of Hormone Replacement Therapy among Breast Cancer Patients and Healthy Controls in Libya with Corresponding Chi-Square Analysis and Statistical Significance

Hormone Replacement Therapy	Breast Cancer Case		Control		Chi square	P value
	Count	%	Count	%		
Yes	19	37.3	1	2.0	19.760	< 0.001
No	32	62.7	50	98.0		

In addition, surgical history (oophorectomy and hysterectomy) was found to be significantly associated with breast cancer risk. Only 7.8% of breast cancer patients reported undergoing oophorectomy or hysterectomy, whereas the majority (90.2%) had no history of such procedures. Statistical analysis revealed a highly significant association (x^2 = 36.26, $p < 0.001$), indicating that women who had not undergone oophorectomy or hysterectomy were at greater risk of developing breast cancer. Hence, these findings suggest that such surgical interventions may exert a protective effect, further emphasizing the complex interplay between hormonal and reproductive factors in shaping breast cancer risk among Libyan women (Table 5).

Table 5. Association of Oophorectomy and Hysterectomy with Breast Cancer Risk among Libyan Women, Including Chi-Square Analysis and Statistical Significance

Oophorectomy and hysterectomy	Count	%	Chi square	P value
Yes	4	7.8	36.255	< 0.001
No	47	90.2		

Finally, family history emerged as another significant risk factor. A positive family history was reported by 21.6% of breast cancer patients compared to only 3.9% of controls, with statistical analysis confirming a significant association (x^2 = 7.141, $p = 0.008$). Thus, women with a family history of the disease were proportionally more likely to develop breast cancer than those without, highlighting the importance of family history as a predictive factor in breast cancer risk assessment within this population (Table 6).

Table 6. Association Between Family History of Breast Cancer and Disease Occurrence among Libyan Women, with Chi-Square Analysis and Statistical Significance

Family History	Case		Control		Chi square	P value
	Count	%	Count	%		
Yes	11	21.6	2	3.9	7.141	0.008
No	40	78.4	49	96.1		

Discussion

Breast cancer is a multifactorial disease influenced by hormonal, genetic, environmental, demographic, and socioeconomic factors, and it continues to cause high mortality rates of around 35% in Egypt and 33% in Libya [13,2]. The results of this study showed no statistically significant correlation between menopausal stage and the incidence of breast cancer. In particular, 60.8% of cases were pre-menopausal, while 39.2% of cases were post-menopausal, suggesting that there is no significant difference in the incidence of breast cancer between the two groups of women. These findings are in line with research conducted in Kuwait by Shamshirian and Alshaibani [14,15] and Bashamakha [16], who also reported a nearly equal distribution, supporting them. However, they contrast with studies conducted in Nigeria and Libya by Boder and Khaial [12, 16], which found higher rates in premenopausal women. Therefore, the evidence from this study indicates that menopausal status is not a strong predictor of breast cancer risk, even though regional and international findings are still inconsistent. This emphasizes the significance of early detection and prevention strategies for both groups.

On the other hand, breast cancer risk was significantly impacted by age at diagnosis. Given that 58.8% of cases occurred in women aged 35 to 50 and that the highest incidence (31%) was seen in those aged 40 to 49, this study confirmed that breast cancer primarily affects younger women in Libya when compared to developed nations. These results are consistent with research from Benghazi, Derna, and Western Libya [12], as well as with international reports from Kuwait and more general meta-analyses [17,18,15] that show a similar trend toward midlife vulnerability. The younger population structure in Libya helps explain the earlier onset, even though some international studies reported that the peak incidence occurred in women

aged 60 and over [19]. In order to improve outcomes and lower mortality in this high-risk group, the study highlights the urgent need for awareness campaigns and early screening programs aimed at women in their thirties and forties.

The lack of significant associations found with age at menarche, age at first pregnancy, education, marital status, economic status, or parity further suggests that family history has a greater impact on breast cancer risk among Libyan women than socioeconomic or reproductive factors [15,18,19]. Contrary to theoretical expectations, breastfeeding did not exhibit a definite protective effect, despite showing a non-significant trend. Furthermore, in line with previous findings, the most frequent lesion seen was a breast mass [12].

The paradox of vitamin D deficiency among Libyan women, despite the country's abundance of sunshine, is primarily due to cultural and lifestyle factors, including darker skin pigmentation, traditional clothing that restricts sun exposure, and inadequate dietary intake because food fortification is not practiced [10]. As a result, vitamin D deficiency is almost twice as prevalent in Arab nations as it is in Western societies. Because vitamin D is essential for the immune system and cellular growth regulation, it has been investigated as a possible risk factor for breast cancer. The results of this study, which is one of the first in Libya to look at serum 25-hydroxyvitamin D [25(OH)D] levels in connection to breast cancer, showed a significant difference between cases and controls. In particular, deficiency was more prevalent in controls (33% vs. 13.7%), while insufficiency was found in 76.5% of cases compared to 62.7% of controls. In contrast to studies like Abbas et al. (2008) [30], where higher vitamin D levels were consistently found in controls, cases notably reported higher supplemental vitamin D intake. Methodological variations, such as the current study's lack of participant matching, may help to explain some of these disparities.

Since some studies show a protective role for vitamin D while others show no association, the evidence regarding vitamin D and breast cancer is still inconclusive. For example, studies conducted in Saudi Arabia, Egypt, and Pakistan support an inverse relationship, demonstrating that low serum 25(OH)D concentrations (<50 nmol/L) increase the risk of breast cancer, especially in postmenopausal women [15, 13, 21, 10]. Similarly, large cohort studies in the U.S. and Europe found no significant association [22, 23, 24], while Bertone-Johnson et al. (2005) found lower mean 25(OH)D levels in breast cancer cases [22]. The inconsistencies across international research thus underscore the need for large-scale, well-controlled studies to elucidate whether maintaining adequate vitamin D levels actually offers protection against breast cancer, even though this study helps to understand the Libyan context.

Although the exact mechanisms are still unknown, this study also found significant correlations between diabetes mellitus, hypertension, and breast cancer. Numerous meta-analyses and cohort studies have linked hypertension to the risk of breast cancer, especially in postmenopausal women [9, 17, 12, 16, 25, 26]. In younger women, long-term use of antihypertensives has been linked to invasive estrogen receptor-positive (ER+) breast cancer [25]. Other research, however, found no correlation [27]. Likewise, studies have consistently linked type 2 diabetes to a 20–27% excess relative risk of breast cancer [31, 32, 15, 33, 17]. The biological explanations for this association include the mitogenic effects of insulin and the overexpression of insulin receptors in breast cancer cells. The overall evidence indicates that both hypertension and type 2 diabetes may contribute to elevated breast cancer risk, particularly in postmenopausal women, despite some studies finding no significant association [34]. This underscores the need for large-scale, controlled studies to elucidate these relationships and inform prevention techniques. In addition, this study shows that using an oral contraceptive pill (OCP) and hormone replacement therapy (HRT) are important predictors of breast cancer, which is in line with earlier findings [18, 35, 5, 36, 14], even though some studies found no correlation [15, 37]. Furthermore, research shows that risk is influenced by the kind and length of HRT [38, 39], although other studies indicate that different formulations may have different effects [39, 40]. Therefore, more research is required to elucidate the distinct impact of hormonal therapies on breast cancer risk, and healthcare providers should carefully consider regimen, duration, and patient profiles. Finally, in support of earlier findings, a positive family history was substantially linked to an increased risk of breast cancer [15, 12, 18, 16]. Thus, routine screening, clinical exams, and self-breast awareness should be prioritized by women with a family history of breast cancer [41]. Breast health education and customized risk assessments are still crucial to guarantee prompt detection and enhance results.

Conclusion

This study evaluated breast cancer risk factors in the Libyan population, revealing that while age, family history, and genetic mutations remain key non-modifiable contributors, other factors such as menopausal status, marital status, education, socioeconomic level, and parity showed no significant associations. The most common age range for breast cancer diagnoses was 35 to 50. Comorbid conditions (diabetes mellitus, hypertension), hormone replacement treatment, and the use of oral contraceptives were found to be significantly associated. Interestingly, vitamin D deficiency seemed to be less common in patients than in

controls, which may indicate a protective function. These results underline the necessity of focused risk assessment and additional study to inform Libya's preventative measures.

Conflict of interest. Nil

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