Original Article

Roles of Biopsychosocial Factors in the Development of Breast Cancer

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ABSTRACT

Objective: The aim of this study was to determine the roles of biopsychosocial risk factors in the development of breast cancer.

Materials and methods: This hospital-based case-control study included 491 women with breast cancer (study group) and 512 women who did not have cancer or other serious diseases (control group). Biological, psychological, and social risk factors were compared between the two groups. Data were collected using the semi-structured interview, the Stress Assessment Form, and the Coping Strategy Indicator to assess these factors.

Results: When the significantly different biopsychosocial variables between the study and the control groups were evaluated together, independent breast cancer risk factors were found as follows: a stressor experienced in the last 5 years, age 40 years and older, inadequate social support perception, use of avoidance coping strategy, being a housewife, having a family history of cancer, and having a body mass index ≥25.

Conclusion: This study showed a relationship between breast cancer risk and manageable variables (obesity, stressor and coping strategy, social support, and employment status), age and family history of cancer, which are biopsychosocial factors. Biopsychosocial aspects are becoming a greater part of many different healthcare systems.

Keywords: Breast cancer, coping, psychosocial stress, risk factors, social support

Introduction

Cancer, a chronic and life-threatening disease, is an important cause of morbidity and mortality. The most common type of cancer diagnosed in women is breast cancer (1). Early recognition of high-risk women is important because of the development of surgical, medical, and oncologic alternatives for breast cancer, every passing year (2). Enlightening factors that contribute to breast cancer to prevent the disease, determine risk groups, and improve early diagnosis or treatment strategies are required.

Even though the etiology of breast cancer was not clearly presented in the past, many epidemiologic risk factor studies have been conducted (3, 4), and many unchangeable and changeable risk factors (lifestyle and psychosocial factors) for breast cancer have been identified. According to some studies, changeable factors are useful for developing preventive strategies for breast cancer (5). However, researching stressful life events independently of factors such as coping style, behavioral pattern, and social support could be a flawed approach. A limited number of studies have examined the effects of these variables on the etiology of breast cancer (5, 6, 7). Socio-economic characteristics as risk factors for breast cancer are also discussed. An opinion suggested that socioeconomic characteristics could be an independent risk factor for breast cancer. Another aspect affecting life style such as reproduction and nutrition may be associated with risk of breast

cancer (8). Several studies have researched risk factors for breast cancer in Turkey (9, 10). However, factors such as social support and coping style were not assessed in association with stress.

It is accepted that multifactorial etiology and processes, play a role in the development of breast cancer (5). Humans are biological, psychological, and social beings in whom the whole is more than the sum of all parts. The interaction between all these dimensions needs to be considered in the etiology of diseases. Therefore, the effect of factors such as sociodemographic and reproductive characteristics, lifestyle, psychological stress, and coping skills should be integrally considered in the development of breast cancer since all these factors are interrelated with each other. This study aimed to determine the roles of biopsychosocial risk factors in women who are diagnosed as having breast cancer.

Material and Methods

Sample and design
This hospital-based case-control survey study was conducted by the Florence Nightingale Breast Working Group and the Consultation Liaison Psychiatry Department, Istanbul Faculty of Medicine, Istanbul University, Istanbul. The working group included 491 patients who received treatment and follow-up between September 2013 - September 2014 and who accepted to participate in the study. The control group included 512 women who accepted to participate in the study; the control group consisted of women who apply to other departments with no serious disease or cancer.

The majority (61%) of participating subjects (491) were within the age range of 40-59. Among the subjects, the educational level of 39% were university or above. However most of those are housewives (51.9%). Among the study group 69.4% were married. As for the control group, 55.7% of those 512 women were within group of 40-59 years of age, the majority (49.8%) of whom had completed education at a university level or above. The percentage of those working happened to be 58.7%. The majority of the women in the control group were married (76.9%).

Data were collected through semi-structured interviews and the stress assessment form developed by researchers to assess biopsychosocial risk factors related to breast cancer (Figure 1) and the Coping Strategy Indicator developed by Amirkhan. The study was approved by the Department of Ethical Committee, T.C. Bilim University and started after the obtaining consent from the patients.

Measures
The semi-structured interview form included data about participants' social support perceptions, healthy life behavioral patterns (height, weight, physical activity level, smoking, and alcohol consumption)**,** medical histories (having chronic physical illness, family history of cancer)**,** reproductive characteristics (age at menarche, oral contraceptive use, birth, abortus, age at first labor, breastfeeding, menopause), and demographic characteristics (age, education, marital status, employment status, economic condition)**.**

The stress assessment form was categorized into four subdimensions to be able to evaluate patients' stressors and their entire life cycles. This form included data about childhood trauma (being raised in a dysfunctional family, taking responsibilities of adults during childhood, divorced parents, loss of mother/father, a serious health problem, negligence, abuse, being subjected to violence), major life events (death of a loved one, job loss, a chronic serious disease, divorce, economic crisis, earth-
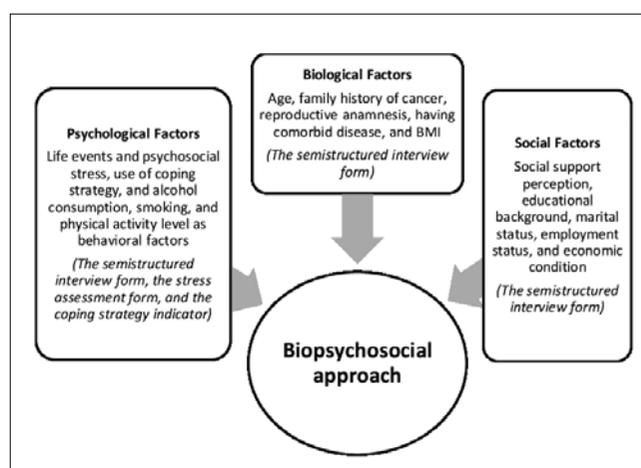

Figure 1. Study design: Biopsychosocial risk factors

quake), having a stressor experienced in adulthood but still effective, to understand whether the chronic stress exists (problems with interpersonal relations, conflict, and economic difficulties), and having an important stressor experienced in the last 5 years of the premorbid period that was continuous and caused immense distress (relationship, work stress, economic problems, or unemployment, death of a loved one).

The Coping Strategy Indicator was developed by Amirkhan (11), and the validity and reliability analyses of the scale in Turkey were performed by Aysan (12). The Coping Strategy Indicator was selected for (1) practical, (2) theoretical, and (3) psychometric reasons. This measure is a relatively brief coping inventory of 33 items. Ratings are made on a 3-point scale anchored at "not at all" and "a lot." This scale consisted of three subscales: problem solving, seeking social support, and avoidance. The first subscale problem solving methods, the second subscale measured the support received for improving interpersonal relations and relaxation methods, and the last subscale assessed the psychological and physical withdrawal. Higher scores obtained from problem solving and seeking social support subscales indicated the use of positive (effective–active) coping strategies. However, higher scores obtained from the subscale of avoidance meant that the patient used negative (ineffective–inactive) coping strategies.

Statistical analysis
Statistical analysis was performed using SPSS version 20.0 (IBM Corp. New York, USA). The body mass index (BMI) was calculated as weight (kg)/height^2 (m^2). The Chi-square test was used in the statistical analyses to evaluate the significant factors associated with breast cancer risk by estimating the odds ratio (OR) and 95% confidence intervals (CI). Logistic regression was used to construct a multivariable model of independent factors associated with breast cancer risk. Forward stepwise regression was used for factor selection, and only factors with a frequency >10% that exhibited univariate significance levels of less than 0.05 were examined. For each factor in the model, the likelihood of breast cancer risk was estimated using the OR and 95% CI. A *p* value of <.05 was considered significant in the statistical analyses.

Results

The univariate analysis of the biological factors determined that the risk of breast cancer was higher for older women than for women aged ≤39 years (40-59 years; OR, 3.82; 95% CI, 2.75–5.30), (≥60 years; OR, 12.92; 95% CI, 8.07–20.70); for patients with a family history of cancer than for those without (first-degree relative: OR,

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2.29; 95% CI, 1.68–3.11; second-degree relative: OR, 1.72; 95% CI, 1.18–2.51); and for patients who experienced early menarche rather than for those whose age at menarche age was ≥14 years (12-13 years: OR, 1.44; 95% CI, 1.09–1.90), (≤11 years: OR, 1.77; 95% CI, 1.06–2.93). It was also higher for patients whose BMI was ≥25 kg/m² (OR, 2.32; 95% CI, 1.79–3.02) and for patients who had a chronic disease (OR, 1.85; 95% CI, 1.40–2.46). The study found that oral contraceptive use (OR, 0.72; 95% CI, 0.53–0.96), not giving birth (OR, 0.48; 95% CI, 0.35–0.67), and not breastfeeding (OR, 0.66; 95% CI, 0.49–0.89) were decreasing factors for breast cancer risk. No significant relationship was found between the development of cancer and age at first labor, abortus, and received infertility treatment. All the biological factors were tested using the logistic regression forward-LR analysis. The analysis yielded independent variables that were entered into the model in each step and the data shown in Table 1 in the third step.

According to the univariate analysis of the psychological factors (existence of distress, coping strategy) and behavioral (smoking and alcohol intake, physical activity level) that could be effective in the development of breast cancer, it was found that with the exception of problem-solving coping strategy and smoking, the researched factors were effective. Of these, having a childhood trauma (OR, 1.48; 95% CI, 1.14–1.91), the existence of a major life event (OR, 1.76; 95% CI, 1.22–2.53), chronic stress (OR, 2.01; 95% CI, 1.52–2.67), having a stressor experienced in the last 5 years of the premorbid period (OR, 3.96; 95% CI, 3.02–5.20), use of avoidance (OR, 1.41; 95% CI, 1.07–1.85), seeking social support (OR, 1.53; 95% CI, 1.17–2.01), and low level of physical activity (OR, 1.36; 95% CI, 1.04–1.77) increased the risk of breast cancer, whereas alcohol consumption (OR, 0.51; 95% CI, 0.39–0.67) had a decreased effect on breast cancer risk. All these factors were tested using the logistic regression forward-LR analysis. The analysis yielded independent variables that were entered into the model in each step and the data shown in Table 2 in the fourth step.

The univariate analysis of the social factors that can be effective in the development of breast cancer risk determined the following factors as social factors that increase breast cancer risk: educational background [higher risk for those who graduated from high school (OR, 1.57; 95% CI, 1.17–2.13) or primary school (OR, 2.19; 95% CI, 1.60–2.99) than for those with a bachelor's degree or higher]; marital status, there was a higher risk for those who were [married (OR, 1.65; 95% CI, 1.12–2.42) or widow/divorced (OR, 3.66; 95% CI, 2.23–5.98)] than in those who were single; employment status, a higher risk was observed in those who were unemployed than employed; [retired (OR, 3.05; 95% CI, 2.12–4.39), housewife (OR, 2.94; 95% CI, 2.20–3.92)]; economic condition, there was a higher risk for those who defined their economic condition as moderate (OR, 1.54; 95% CI, 1.17–2.03) or low (OR, 2.99; 95% CI, 1.79–5.01) than as good; and perception of inadequate social support (OR, 2.92; 95% CI, 1.58–3.04). All these factors were tested using logistic regression forward-LR analysis. The analysis yielded independent variables that were entered into the model at each step and the data shown in Table 3 in the fourth step.

In conclusion, when the biological, psychological, and behavioral factors were separately tested using the logistic regression forward-LR analysis, it was found that the breast cancer risk was associated with advanced age, BMI (>25 kg/m²), family history of cancer, existence of a stressor experienced in the last 5 years of the premorbid period, use of avoidance and seeking social support coping strategies, having a chronic stressor, unemployment, inadequate social support, being widow/divorced, and low economic condition ($p \leq 0.04$). When these biopsychosocial factors were tested using logistic regression forward-LR analysis, independent variables that were obtained that were entered into the model in each step and the data shown in Table 4 in the seventh step.

Discussion and Conclusion

Many factors have an effect on the development of breast cancer. These include age, family history of cancer, reproductive factors, lifestyle, and psychosocial factors (13). This study evaluated the biological, psychological, and social factors together and determined that the existence of a stressor experienced in the last 5 years of the premorbid period,

Table 1. Multivariable model: biological factors related to the risk of breast cancer

Variables		B	S.E.	p-value	OR	95% CI for EXP(B) Lower-Upper
Age (years)				<.0001		
≤39	(ref.)				1	
40–59		1.103	.210	<.0001	3.014	1.999-4.544
≥60		1.994	.291	<.0001	7.345	4.152-12.993
The body mass index (kg/m2)						
≤24.99	(ref.)				1	
≥25		.501	.168	.003	1.650	1.188-2.291
Family history of cancer				.004		
No	(ref.)				1	
First-degree relative		.606	.197	.002	1.833	1.246-2.695
Second-degree relative		.475	.239	.04	1.608	1.007-2.569

B: Regression coefficient; SE: Standard Error; OR: odds ratio; 95% CI: 95% confidence interval; ref: reference

Table 2. Multivariable model: psychological and behavioral factors related to the risk of breast cancer

Variables	B	S.E.	p-value	OR	95% CI for EXP(B) Lower-Upper
Stressor experienced in the last 5 years					
No (ref.)				1	
Yes	1.495	.171	<.0001	4.459	3.190-6.233
Avoidance coping strategy					
No (ref.)				1	
Yes	.419	.164	.01	1.521	1.103-2.097
Seeking social support coping strategy					
Low (ref.)				1	
High	.390	.163	.01	1.477	1.073-2.034
Chronic stressor					
No (ref.)				1	
Yes	.365	.184	.04	1.441	1.005-2.066

B: Regression coefficient; SE: Standard Error; OR: odds ratio; 95% CI: 95% confidence interval; ref: reference

Table 3. Multivariable model: social factors related to the risk of breast cancer

Variables	B	S.E.	p-value	OR	95% CI for EXP(B) Lower-Upper
Employment status			<.0001		
Working (ref.)				1	
Retired	1.041	.172	<.0001	2.832	2.023-3.965
Housewife	.828	.210	<.0001	2.290	1.516-3.458
Social support perception					
Sufficient (ref.)				1	
Insufficient	.700	.183	<.0001	2.014	1.405-2.885
Marital status			.001		
Single (ref.)				1	
Married	.425	.236	.072	1.529	0.963-2.428
Widowed/Divorced	1.108	.297	<.0001	3.027	1.691-5.421
Economic condition					
Good (ref.)				1	
Moderate	.364	.293	.214	1.438	0.810-2.557
Low	.699	.309	.02	2.012	1.096-3.690

B: Regression coefficient; SE: Standard Error; OR: odds ratio; 95% CI: 95% confidence interval; ref: reference

perception of inadequate social support, use of avoidance and seeking social support coping strategies, being a housewife, family history of cancer, advanced age, and BMI ≥25 kg/m² increased the risk of breast cancer.

Age (13) and family history of breast and/or ovarian cancers (13, 14) are the most known risk factors for breast cancer. In line with these studies, present study implied that having a first-degree relative with breast cancer and being more than 40 years distinctly increased risk. The other most frequently researched risk factors are reproduction and obstetric history variables. Various studies have found that there exists a relationship between early menarche (10, 13), advanced maternal age (10, 13), and breast cancer. The protective role of breastfeeding in breast cancer is also included in the literature (2, 15). Iqbal et al. (16) demonstrated no correlation between breast cancer risk and labor, age at first labor, and breastfeeding. The present study also found no differ-

Table 4. Multivariable model: biopsychosocial factors related to the risk of breast cancer

Variables	B	S.E.	p-value	OR	95% CI for EXP(B) Lower-Upper
The stressor experienced in the last 5 years					
No (ref.)				1	
Yes	1.734	.208	<.0001	5.662	3.767-8.511
Age (years)			<.0001		
≤39 (ref.)				1	
40–59	1.229	.251	<.0001	3.416	2.090-5.585
≥60	2.487	.401	<.0001	12.024	5.482-26.375
Social support perception					
Sufficient (ref.)				1	
Insufficient	.773	.234	.001	2.166	1.371-3.424
Avoidance coping strategy					
No (ref.)				1	
Yes	.632	.200	.002	1.882	1.271-2.785
Employment status			.002		
Working (ref.)				1	
Housewife	.688	.227	.002	1.989	1.275-3.103
Family history of cancer			.006		
No (ref.)				1	
First-degree relative	.660	.241	.006	1.934	1.207-3.101
The body mass index (kg/m2)					
≤24.99 (ref.)				1	
≥25	.444	.206	.03	1.559	1.042-2.333

B: regression coefficient; SE: standard error; OR: odds ratio; 95% CI: 95% confidence interval; ref: reference

ence between the controls and the study group in terms of age at first labor, and high level of labor, and breastfeeding experience in patients with breast cancer; this might be because the control group comprised of young and single women. Various studies that researched the relationship between breast cancer and abortus (15), and the use of oral contraceptives (10, 14, 15) reported that these factors could increase breast cancer risk. The multivariable analysis of the present study did not determine factors related to reproduction and obstetric history as independent risk factors. Contradictory results might be obtained because reproductive factors are influenced by certain variables such as demographics, culture, and subtype of breast neoplasm. Presence of chronic diseases such as diabetes and hypertension was also found to be a risk factor for breast cancer (2, 10); the findings of the present study are consistent with the published reports. The effect of obesity on breast cancer was examined with diet or BMI, and similar to the results of the present study, many studies (5, 16) found a relationship between BMI ≥25 kg/m² and risk increase in the development of breast cancer. When the biological factors were assessed separately or along with the biopsychosocial factors, it was seen that advanced age, obesity, and a family history of cancer were independent and significant risk factors in the development of breast cancer.

It is a common belief in society that stress is a risk factor for cancer, espe-

cially for breast cancer. Various studies that explored the effect of psychological factors on the development of breast cancer have been published in the literature. Important variables such as the number and type of adverse life events and the time of exposure to stress and methodologic differences led to contradictory findings (4). Consequently, the stress assessment form was developed to assess an individual's childhood period, source of major and chronic stressors in adulthood, and important stressors experienced in the last 5 years. The univariate analysis found that a trauma experienced during childhood was associated with breast cancer; other studies also reported similar findings (17). Ginzburg et al. (18) determined similar childhood experiences of the participants in the study and control groups. The present study also found that a trauma experienced during childhood was not an independent risk factor in the multivariate analysis. Three meta-analyses that assessed the relationship between breast cancer and stress between 1966 and 2007 presented inconsistent results and suggested the lack of evidence remarking the diversity of research designs; however, it was stated that the correlation between breast cancer risk and stressful life events could not be ignored (19, 20, 21). Although the univariate analysis performed on the present study determined major life events, chronic stress, and having a stressor experienced in the last 5 years as risk factors, the logistic regression analysis of the psychological variables did not find major life events as an independent risk factor. Having a stressor experienced in the last 5 years

among the biopsychosocial variables was determined as an independent variable that considerably increased the risk of breast cancer. A study conducted in Turkey by Ceber et al. (9) found no difference between the study and control groups in terms of the degree of stressor experienced in the last 5 years. On the other hand, similar to the results of the present study, it was reported that the self-reported stress in the last 5 years (15, 22, 23), having a stressful vital event in the last 2 years (24), and having stressful life events before the diagnosis (25) were associated with breast cancer.

The effect of stressful life events was related with the type and time of the event, and with how it was coped. This study determined that inadequate social support, use of avoidance and, seeking social support methods increased breast cancer risk. The possible benefits of effective stress coping strategy and of social support on health care, life quality, and immunity are well known (7, 26). Studies conducted on women with breast cancer and the effect of social support and coping strategies focused on the period after cancer diagnosis and reported that these played a role in decreasing distress, and adaptation to the disease (26). A limited number of studies are available about the effect of coping styles and social support on the development of breast cancer; both studies were conducted many years ago, and this issue was not adequately researched. Edwards et al. (27) reported that the correlation between breast cancer and life events was not moderated by coping or availability of social support. Geyer (6) proposed social support as modifying the effect of stressful life events. Chen et al. (25) reported a significant increase in breast cancer risk for women experiencing a severely threatening life event and confronting stress by focusing on the problem at hand. However, it was stated that this interaction was not clear and hence should be tested using a multivariate model. Price et al. (7) concluded that stress did not cause breast cancer in women, but the absence of intimate emotional support could increase the vulnerability to this disease. Ollonen et al. (28) reported a moderate level of relationship between the increasing breast cancer risk and defense mechanisms, and inadequate coping. The study explained the biological effect of defense and coping strategies on cancer; these can directly affect hormonal, immune, and nervous system functions, or indirectly through behaviors such as alcohol intake, smoking, nutrition, and physical activity. The multivariate analysis in our study assessing the stated behaviors did not determine these behaviors as important risk factors. The present study results showed that perception of inadequate social support and use of avoidance coping mechanism were independent variables related to breast cancer. Further studies are required to elucidate the underling mechanisms of these factors.

The incidence of breast cancer varies with developmental level of the country and ethnicity. Economic condition, educational background, employment status, and marital status are important sociocultural variables. The univariate analysis of this study determined a significant relationship between breast cancer and these factors, and the regression model found that housewives had a higher risk of breast cancer. A study conducted in Pakistan by Anjum et al. revealed similar results (29). Othieno-Abinya et al. (14) conducted a study in Kenya; the regression analysis of the study determined that breast cancer was less prevalent in housewives and unemployed women, with no difference in terms of education and marital status. Conflicting conclusions are reported in the literature. It appears that the risk posed by becoming a housewife for developing breast cancer is coincidental. Taking this into consideration, it would be appropriate for this matter to be researched using a different methodology. The studies comparing the

effect of social and economic status on the outcome focused mainly on the level of education and income. It was found in the literature that women who had higher education and income at the individual and social levels had a higher risk of breast cancer (15, 30). Some studies examined the relationship between work stress and breast cancer, but no difference was found (31). Furthermore, unemployed women had lower education and income level, and it was associated with the absence of socioeconomic support.

Breast cancer is a disease that has a multifactorial etiology and these factors interact with each other. Biopsychosocial aspects are becoming a greater part of many different healthcare systems. The present study showed a relationship between breast cancer risk and manageable variables (obesity, stressor and coping strategy, social support, and employment status), age and family history of cancer, which are biopsychosocial factors. It was also found that having a stressor experienced in the last 5 years was an independent and significant risk factor. Assessing factors such as coping and social support together, which can change the effect of stressful life events, is important while researching the effect of stress. Conducting large-scale case-control prospective studies and researching the effect of stress using biological parameters will be helpful in the future.

The present study had certain limitations. Firstly, this was a retrospective study. Women's lifestyles can change before and after cancer diagnosis; therefore, it can be harder to objectively assess life events. Secondly, this study used self-report surveys, and the sample group did not reflect all Turkish women. Despite the aforementioned limitations, the strength of this study was that it evaluated many biopsychosocial factors together.

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