
RESEARCH COMMUNICATION

The Role of Depression in the Development of Breast Cancer: Analysis of Registry Data from a Single Institute

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Abstract

Although controversial, the belief that developing breast cancer may be associated with psychological distress is not uncommon. The present study examined the role of psychological variables in the development of breast cancer in women attending a breast clinic for medical examination in Tehran, Iran. During a three-year period (1997-1999) a trained female nurse interviewed all women attending the Iranian Center for Breast Cancer (ICBC) before a confirmed diagnosis was made (N = 3000). Data were collected on demographic variables (age, education and marital status), known risk factors (age at menarche, age at first time full term pregnancy, family history of breast cancer, menopausal status, and oral contraceptive use), psychological variables, including history of psychiatric medications, depression (depressed mood, hopelessness, and loss of interests and pleasures), anxiety (mental and somatic signs) and two single measures of overall health and quality of life. In all, 243 patients were diagnosed as having breast cancer. A total of 486 patients with benign disease were randomly selected from the original cohort as controls. Univariate and multivariate logistic regression analyses were performed to determine the predictive effect of each factor on the risk of breast cancer. There were no significant differences between cases and controls except for age at menarche (P = 0.007) and family history of breast cancer (P < 0.001). With regard to psychological variables studied, the results showed that there were significant differences between cases and controls regarding depression (depressed mood P < 0.0001, hopelessness P = 0.001, and loss of interest and pleasures P = 0.001), and anxiety (mental signs P = 0.006). Finally, after performing multiple logistic regression analysis in addition to family history and age at menarche, depressed mood and hopelessness showed significant results (odds ratios of 1.90, and 1.63 respectively). The findings of the present study suggest that in addition to the known risk factors, psychological determinants such as depressed mood may play an important role in etiology of breast cancer and deserve further investigation, especially in different populations.

Key Words: Breast cancer - Case-control study - Depression - Risk factors - Iran.

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Introduction

The belief that developing breast cancer may be associated with psychological distress is not uncommon (Cassileth, 1996). Early studies on this issue often indicated a positive causal relationship between psychological factors and breast cancer (Chen et al., 1995). Studies have shown psychological and social experiences such as emotional repression, loneliness, and loss or early and chronic stress to be strongly related to breast cancer (Fox et al., 1994; Jacobs and Bovasso, 2000). However, it has been argued that the methodological flaws in such studies are self-evident and that well-designed studies do not support the hypothesis

that psychological factors are associated with onset of breast cancer (Protheroe et al., 1999). Furthermore, with regard to stressful life events and risk of breast cancer a recently published meta-analysis of literature indicated that the hypothesis of a casual relationship between adverse life events and onset of breast cancer could not be supported. The review confined itself only to the role of adverse life events in causing breast cancer and therefore did not rule out the possibility that stress may exert other influences on breast cancer (Petticrew et al., 1999). In addition a more comprehensive review on empirical evidence for a relationship between stressful life events, coping style, social support and emotional and personality factors concluded that

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the evidence for a relationship between psychosocial factors and breast cancer is weak. The review indicated that the strongest predictors were emotional repression and severe life events (Butow et al., 2000). Despite such findings, speculation about this relationship still exists and a survey of 150 health professionals found that almost half were either undecided or confident that there is a role for stress in the etiology of breast cancer (Steptoe and Wardle, 1994). In

general, all studies under review were from the western culture and there were no studies from other cultures. The present study was therefore performed to examine the role of psychological variables in the development of breast cancer in women attending a breast clinic for medical examination in Tehran, Iran. It was thought that a study from a developing country might contribute to the existing knowledge on the topic.

Table 1. The Characteristics of Breast Cancer Cases and Benign Disease Controls and Risk Factors Derived from Univariate Logistic Regression Analysis

	Breast cancer (n = 243) No. (%)	Control group (n = 486) No. (%)	OR (95% CI)	P value
Age (year)				
Mean (SD)	46.6 (11.2)	45.5 (10.1)	1.01 (0.99-1.02)	0.18*
Education				
Illiterate	43 (18)	94 (19)	1.00 (ref.)	
Primary	71 (29)	129 (27)	1.20 (0.75-1.91)	0.43
Secondary	78 (32)	163 (33)	1.05 (0.66-1.64)	0.84
Higher education	51 (21)	100 (21)	1.12 (0.68-1.83)	0.66
Marital status				
Married	204 (84)	421 (87)	1.00 (ref.)	
Single	10 (4)	24 (5)	0.86 (0.40-1.83)	0.69
Widowed/divorced	29 (12)	41 (8)	1.46 (0.88-2.41)	0.14
Age at menarche (year)				
Mean (SD)	13.2 (1.4)	13.5 (1.3)	0.85 (0.75-0.95)	0.007*
Age at first time full term pregnancy (year)				
Mean (SD)	21.8 (4.5)	21.3 (4.2)	1.02 (0.98-1.06)	0.18*
Menopausal status				
No	167 (69)	356 (73)	1.00 (ref.)	
Yes	76 (31)	130 (27)	1.24 (0.89-1.74)	0.20*
Family history of breast cancer				
No	206 (85)	454 (93)	1.00 (ref.)	
Yes	37 (15)	32 (7)	2.54 (1.54-4.21)	< 0.001*
Oral contraceptive use				
No	127 (52)	286 (59)	1.00 (ref.)	
Yes	116 (48)	200 (41)	1.31 (0.96-1.78)	0.09*
Depressed mood				
No	204 (84)	451 (93)	1.00 (ref.)	
Yes	39 (16)	35 (7)	2.46 (1.51-4.01)	< 0.001*
Hopelessness				
No	190 (78)	428 (88)	1.00 (ref.)	
Yes	53 (22)	58 (12)	2.05 (1.36-3.10)	0.001*
Loss of interest and pleasures				
No.	194 (80)	431 (89)	1.00 (ref.)	
Yes	49 (20)	55 (11)	1.98 (1.30-3.01)	0.001*
Anxiety (mental signs)				
No	174 (72)	392 (81)	1.00 (ref.)	
Yes	69 (28)	94 (19)	1.65 (0.97-2.67)	0.006*
Anxiety (somatic signs)				
No	213 (88)	447 (92)	1.00 (ref.)	
Yes	30 (12)	39 (8)	1.61 (0.97-2.67)	0.06*
History of psychiatric medications				
No	203 (84)	419 (86)	1.00 (ref.)	
Yes	40 (16)	67 (14)	1.23 (0.81-1.88)	0.33
Overall health				
Mean score (SD)	4.9 (1.4)	4.9 (1.2)	0.99 (0.88-1.11)	0.91
Overall quality of life				
Mean score (SD)	5.2 (1.5)	5.3 (1.3)	0.97 (0.87-1.08)	0.64

* variables that entered into multivariate logistic regression analysis.

Methods

During a three-years period (1997-1999) a trained female nurse, supported by a panel of specialists, interviewed all women attending the Iranian Centre for Breast Cancer (ICBC) before a confirmed diagnosis was made (N =3000). Data were collected on demographic variables (age, education and marital status), known risk factors (age at menarche, age at first time full term pregnancy, family history of breast cancer, menopausal status, and oral contraceptive use), psychological variables including history of psychiatric medications, depression (depressed mood, hopelessness, and loss of interests and pleasures), anxiety (mental and somatic signs), and two single measures of overall health and quality of life using a seven point scale ranging from 1 (very poor) to 7 (excellent). Psychological data were collected based on characteristics derived from the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders, DSM-IV, (American Psychiatric Association, 1994).

In all, 243 patients were diagnosed as having breast cancer. A total of 486 patients with benign breast disease were randomly selected from the original cohort as controls (two controls per case). This was to ensure adequate power for the study. To analyze data a similar method to the previous studies was used (Protheroe et al., 1999). First, to estimate odds ratios, univariate logistic regression was performed to indicate the predictive effect of each factor on the risk of breast cancer. Then, the factors which were significant ($P < 0.25$) were entered into a forward selection multivariate logistic regression analysis.

Results

The characteristics of breast cancer cases and benign disease controls are shown in Table 1. There were no significant differences between cases and controls except for age at menarche ($P = 0.007$) and family history of breast cancer ($P < 0.001$). With regard to psychological variables studied, the results as shown in Table 1 indicated that there were significant differences between cases and controls in depression (depressed mood $P < 0.0001$, hopelessness $P = 0.001$, loss of interest and pleasures $P = 0.001$), and anxiety (mental signs $P = 0.006$), while overall health and quality of life were not.

Finally performing multiple logistic regression analysis, the results indicated that only four variables were

independently significant predicting factors for developing cancer. These were age at menarche and family history of breast cancer, depressed mood and hopelessness. The other variables that entered into the model did not show any significant results. The final model is shown in Table 2.

Discussion

This prospective study indicated that psychological stress might have a role in development breast cancer. The most important feature of this study was that it only dealt with psychological distress rather than stressful life events. In addition, consistent with our previous findings from earlier study on the risk factors for breast cancer in Iran (Ebrahimi et al., 2002), also a strong association between family history of breast cancer and risk of developing breast carcinoma was observed. All other factors studied, although not significant, showed clear patterns in odds ratios for most variables.

There have been several explanations to help to understand the complex relationship between psychological distress and the risk for developing breast cancer. This study did not intend to investigate such relationships but it is argued that life event stress, personality and social support influence an individual's ability to cope, which in turn could mediate breast cancer risk via alterations in neuroendocrine and immune functioning (Hilakivi-Clarke et al., 1993). A recent study very similar to present investigation found no evidence to support an independent association between anxiety and depression and the development of breast carcinoma (Price et al., 2001b). However, the same study in a companion paper concluded that although there was no evidence of an independent association between life event stress and breast carcinoma, the findings provided strong evidence that social support interacts with highly threatening life stressors to increase the risk of breast cancer significantly (Price et al., 2001a). Thus, the findings from this study should be interpreted in the light of models and theories discussed.

In the final model the study findings indicated that only depressed mood and hopelessness were related to the risk of breast cancer. The other psychological factors studied (loss of interest and pleasures, and anxiety) although in the univariate analysis were significantly associated with the risk of developing breast cancer, in the final model were no longer significant. This is similar to the findings from the literature where it has been shown that emotional repression or hopelessness could be regarded as strong predictors of developing cancer in general and breast cancer in particular (Butow et al., 2000; Everson et al., 1996). This however implies that the mind-body relationship in cancer could not be neglected (Dalton et al., 2002).

The findings from this study are not clear-cut. There were several limitations. The case-control nature of the study and the lack of information on some other known risk factors are to name but a few. However, there were strengths adherent to the study including the prospective design, and controls were selected from the same cohort of women

Table 2. Final Main Effects of Risk Factors for Breast Cancer Derived from Multivariate Logistic Regression Analysis

Covariates	Odds ratio (95% CI)	P value
Age at menarche	0.86 (0.76-0.97)	0.01
Family history of breast cancer	2.48 (1.48-4.14)	0.001
Depressed mood	1.90 (1.12-3.22)	0.01
Hopelessness	1.63 (1.05-2.56)	0.03

attending the breast clinic, all interviews was carried out before confirmed diagnosis, and a sufficient sample size was attained.

In conclusion, although controversial, the findings from the present study suggest that in addition to the known risk factors, psychological determinants such as depressed mood may play an important role in etiology of breast cancer and thus deserve further investigation, especially in different ethnic populations.

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