Stressful Life Events as Risk Factor of Breast Cancer in Women

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The present study examined the role of stressful life events as risk factor in the etiology of breast cancer in women. The sample consisted of 100 married women having different symptoms of breast cancer referred by physicians to Institute of Radiotherapy and Nuclear Medicine of Peshawar, Khyber Pakhtunkhwa, Pakistan. The age range of the sample was 45 to 68 years and belonged to upper middle, middle, and lower middle socioeconomic class. Convenience sampling technique was used to select the sample. The Social Readjustment Rating Scale (Holmes & Rahe, 1967) was used to assess the number of stressful life events that had occurred before diagnosis in the past 12 years. As being informed about the final breast cancer diagnosis, patients might be more prone to report their prior stress in an effort to explain their disease. To avoid this recall bias, all the women were interviewed before the final diagnosis (clinical examination, biopsy, & mammography). The chi-square analyses were computed to test the significance of difference between the two groups, that is breast cancer and healthy participants after the final diagnosis. Results showed that breast cancer women reported significantly higher number of stressful life events than the healthy participants. Results further demonstrated that breast cancer women perceived higher levels of stress due to these events than the healthy participants. The findings conclude that adverse life events and the resulting stress on account of these events may represent a risk factor for breast cancer in women.

Keywords. Stressful life events, risk factor, breast cancer.

The diagnosis of breast cancer is a major life stressor for many women (Bower, Crosswell, & Slavich, 2014) with up to 80% of women report significant stress at the time of diagnosis and treatment

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(Flint, Baum, Episcopeo, & Knickelbein, 2013). Although a number of risk factors for breast cancer have been identified, still there remain gaps in current knowledge on the etiology of this disease. Among a number of risk factors studied, some are related to female hormones and reproductive health (Key, Verkasalo, & Banks, 2001). Life style factors such as smoking, alcohol consumption, obesity and lack of physical exercise are known to be the main risk factors for sporadic breast cancer (Mannist et al., 1996). Psychological traumas such as stressful life events also appear to be the most important (Dujits, Zeegars, & Borne, 2003).

Life events are changes occurring in one's life that are either positive or negative (Paykel, 2001). Stress refers to physical, behavioral, emotional and cognitive responses one makes to a disruptive internal or external event. Stressful life events include physical stressors such as infections, physical injuries, pathogens, autoimmunity, and toxin. Psychological traumas relate to stressful environment in home, neighborhood or in workplace. One's ability to habituate or adjust to stress is determined by the way he/she perceives a stressful life event (Paykel, 2001).

Clinical observation has long been suggesting an association between stressful life events and the occurrence of cancer (LeShan, 1959; LeShan & Worthington, 1956). Berrois (1988) taking into account the Hippocrates's theory of bodily humor (1956) studied the life history and found breast cancer more often in melancholy (black bile), anxious, and depressed women. LeShan, Worthington, and Bahnson (1969) on the basis of their experiences were convinced that malignant processes were associated to certain psychodynamic states. In an early study, LeShan and Worthington (1956) studied patients with malignant diseases and found an association between cancer and lost relationship prior to diagnosis. In 1955, Selye developed a model called the general adaptation syndromes having three stages, that is, alarm, resistance, and exhaustion. According to Selye (1955), prolonged stress would eventually exhaust the response capacity of the individual and result in diseases (the work which evolved the concept of homeostasis).

The levels of hormones, neurotransmitters, and immune normally fluctuate in a short and medium time framework. Various physical events such as acute hunger, infection or imminent danger disrupt these functions, and as the events resolve, equilibriums re-established. However, the psychological events (traumatic experiences) result into long lasting changes in these physiological processes, including the stress hormones (cortisol) that may lead to allostatic load (McEwen, 2000). Excessive allostatic load according to the allostatic theory

increases the risk of various diseases including breast cancer (Parente, Hale, & Palermo, 2012).

Numerous researches established association between stressful life events and risk of breast cancer (Chen et al., 1995; Lillberget al., 2003; Paleshet al., 2007). In a meta-analysis the researchers found that stressful life events are associated with increased risk of breast cancer (Duijts, Zeegars, & Borne, 2003). Some researches emphasize timing and duration of the stressful life events as an important factor in determining their effect on breast cancer. For example, Jacobs and Bovasso (2000) studied 1,213 women with average age of 43 years at baseline and followed up to14-16 years. The results showed increased risk of breast cancer in women having experienced maternal death in childhood or lifelong depression. Eskelinen and Ollonen (2010) in a study in Finland found that breast cancer women reported more severe losses and cumulative stress in childhood and adolescence than women with benign breast diseases. In another study, Ollonen, Lehtonen, and Eskelinen (2005) examined stressful life events and risk of breast cancer in 115 women before diagnosis. Their findings revealed that breast cancer participants compared to the healthy women and those having benign breast disease reported significantly more severe losses and stressful life events in the past 10 years. Geyer (1991) found short time period between initial diagnoses of breast cancer and its recurrence or metastasis for the women having experienced stressful life events in the past life.

Cardinal, Ortiz-Tallo, Frias, and Lozano (2008) examined stressful life events and subjective well-being in 58 women diagnosed with breast cancer and 60 healthy (matched) controls. Their result revealed that breast cancer women reported more stressful life events in the last two years than the healthy participants. Further, these women experienced higher level of neuroticism and anger than the controls. In an earlier research, women reported strong belief that stress is an important psychological factor in the onset of their breast cancer (Brinton, Malone, Liff, & Schoenberg, 1995). Other researchers found higher number of stressful events before the onset of uni-polar depression in clinical population (Paykel, 2001).

Breast cancer is one of the major causes of death in women worldwide (World Health Organization [WHO], 2009). According to the WHO (2009) estimate among all cancer diagnosed worldwide, 105 represents breast cancer and it constitutes 22% of all new cancers in women, making it the most common cancer in female. Compared to other countries, in Pakistan, there is a highest rate of breast cancer as approximately 0.3 million women in the country out of which 40,000 cases from Khyber Pakhtunkhwa (The Express Tribune, 2015,

December 20), while, in another recent report Pakistan has the highest incidence of breast cancer in Asia resulting 40,000 deaths every year (The Daily Times, 2016, November 1). One out of every nine women are likely to suffer from this disease at any point in life and about 77% invasive breast cancer occurred in women above 50 years, but if diagnosed early the survival rate approach 90% (The Daily Times, 2009, April 26). These mentioned facts, beyond any doubt, suggest that in Pakistan, cancer contributes significantly to mortality. On account of its increased frequency, a host of research has focused to identify the possible risk factors that play an important in its etiology. Among various psychological factors that may increase the risk of breast cancer or influence its progression, one is the stressful life events. The present study, therefore, was designed to investigate if stressful life events play a significant role in the etiology of breast cancer in women of Khyber Pakhtunkhwa Peshawar, Pakistan.

Hypotheses

To examine the role of stressful life events as risk factor for breast cancer in women, the following hypotheses were formulated:

1. Participants having diagnosed with breast cancer would experience high number of stressful life events than the healthy controls.
2. Women diagnosed with breast cancer would obtain higher life change score (perceived stress) than the healthy participants.

Method

Participants

The sample consisted of 100 married women having symptoms of breast cancer such as lump or pain in breast or armpit, pain in collarbone, discharge of fluid or blood from breast nipple, swelling on or redness around or near the nipple or any other abnormality, and had been referred by physicians to the Institute of Radiotherapy and Nuclear Medicine (IRNUM) of Peshawar, Khyber Pakhtunkhwa, Pakistan. Convenience sampling technique was used to select the sample. The age range of sample was 45-68 years (M = 51.5, SD = 9.26) but maximum respondents fall between 51-56 years

(38.03%).The participants belonged to three categories of middle socio-economic status classified on the basis of monthly income. The minimum educational level of the sample was primary level (6 years of schooling) to read only the Quran (Table1).Women having other serious diseases, such as cardiovascular diabetes, hepatitis, or were taking any ant-depressant drugs were not included. The demographic characteristics are shown in Table 1.

Table 1

Demographic Characteristics of the Sample (N = 100)

Demographics	Participants with Breast Cancer (n = 58)		Healthy Participants (n = 42)	
	f	%	f	%
Age (years)				
45-50	08	13.79	10	23.80
51-56	22	38.03	19	45.23
57-62	21	36.20	13	30.95
63-68	07	12.06	–	–
Total	58	100	42	100
Education				
Primary	23	39.65	22	52.38
Middle	05	8.62	10	23.80
Metric	05	8.62	04	09.52
Read Quran only	22	38.03	05	11.90
Illiterate	03	5.17	01	2.38
Total	58	100		100
Socioeconomic Status				
Upper middle	17	29.31	10	23.80
Middle	19	32.75	17	40.47
Lower middle	22	37.93	15	35.71
Total	58	100	42	100

Results in Table 1 show that majority of breast cancer women fall in the age range of 51-56 years (38.03%). The educational level of 39.65% breast cancer women is primary, while 38.03% can read the Quran only. Among the whole sample of breast cancer women 37.93% belonged to the lower middle class and 29.31% belonged to the upper middle class.

Instruments

Social Readjustment Rating Scale (SRRS). It was developed by Holmes and Rahe (1967) and consists of 43 common life time events. The participant is asked to report which life events on given list

occurred in past years prior to an assigned date. To each life event a value or Life Change Score (LCS) is assigned which reflects severity of self-perceived stress the event caused in the participants. Total LCS is obtained by adding LCS corresponding to events occurred in past life of the respondent. LCS of 150 or less indicates low level of stress and 30% chance of developing stress related disorders, 150-299 suggests 50% chances, while 300 plus suggest high levels of stress and 80% chances of getting sick in near future. If an event has occurred or is expected to occur more than once in near future then assigned score is multiplied by frequency of the event.

In present study 150 LCS was used as a cutoff score. The temporal stability (reliability) of the scale was assessed by administering the scale to psychiatric outpatients' and controls during 3 sampling periods over 2 years' time period. Correlations computed for ranking order of life events were consistent for both controls (r = .96 to .89) and patients (r = .91 to .70) as reported by earlier researchers (Gerst, Grant, Yager, & Sweetwood, 1978). The range of correlations to weights assigned was .83 to .59 for controls and .41 to .08 for patients; respectively, suggesting that perceptions of the impact of life change of controls was temporally stable than patients (Gerstet al.,1978). Validity of the scale was assessed by administering the test to 2,500 US sailors to rate their previous 6 months life events and correlating the scores with next 6 months record of their health resulting in significant correlations (Rahe, Mahan, & Arthur, 1970).

Personal data sheet. It was used to obtain the demographic information about the participants regarding age, education, socioeconomic status, and number of children.

Procedure

Written consent was taken from each woman and from the hospital authority. Before any diagnostic procedures were done, women were individually interviewed. Participants reported specific life events that occurred 12 years before diagnosis. For this purpose three recall tests of the adverse life events were taken from each participant. In first test, events that had occurred two years before diagnosis were reported. In second test, events that were experienced two to seven years before diagnosis were recalled. In third recall, participants reported events which had occurred 12 years before diagnosis. The scale was thus, administered three times on each participant with different time periods in mind. As recall of intensity of the stress caused by an event becomes less reliable with increase in time period, (e.g., life time); therefore,

recall test of the events experienced 12 years before diagnosis were taken. The purpose was to examine if they had any negative impact on the participants' vulnerability to breast cancer. When diagnosis was confirmed, participants were divided into two groups, that is, with breast cancer and healthy participants (not diagnosed with cancer) and number of stressful events reported was counted for both groups (with breast cancer & healthy participants). To assess severity of perceived stress, LCS assigned to corresponding events were added and total LCS for each participant was obtained.

Results

The chi-square and independent sample t-test analyses were computed to test the significance of difference between the two groups, that is, breast cancer patients and healthy participants after the final diagnosis.

Table 2

Number of Stressful Life Events in Three Recall Tests by Breast Cancer and Healthy Participants on SRRS (N = 100)

Groups	Recall of Number of Stressful Life Events				χ^2	p
	1st $f(\%)$	2nd $f(\%)$	3rd $f(\%)$	Total $f(\%)$		
Breast Cancer ($n = 58$)	717(12.36)	648(11.17)	584(10.06)	1949(33.60)	91.83	.00
Healthy Control ($n = 42$)	340(8.09)	326(7.76)	280(6.66)	946(22.52)		

Note. Values given in parentheses represent percentage.

Results in the Table 2 show significant difference in the breast cancer and healthy participants. Breast cancer women recall significantly higher number of stressful life events in three tests of recall than the healthy participants.

Independent sample t-test was calculated to determine the mean difference between participants with breast cancer and healthy participants on life change scores in third recall. Results revealed significant difference ($t = 9.23$, $df = 98$, $p < .00$) between the two groups of women. Compared to the healthy participants ($M = 62.50$, $SD = 20.79$), higher mean scores were obtained by the participants with breast cancer women ($M = 165.70$, $SD = 15.57$) suggest higher levels of stress in these women and differed from other group with large effect size (Cohen's $d = .66$).

Table 3

Most Frequently Reported Events by Breast Cancer and Healthy Participants (N = 100)

	Participants with Breast Cancer ($n = 58$)		Healthy Participants ($n = 42$)	
Nature of Stressful Life Events	f	%	f	%
Death of Close Family Member	10	17.24	5	12.00
Change in Health of Family Member	8	13.80	4	9.52
Death of Spouse	5	8.62	2	4.76
Death of Close Friend	4	6.90	2	4.76
Change in Financial State	3	5.17	2	4.76
Divorce and Marital Separation	2	3.45	–	–
Total Events Experienced	30	51.72	15	35.71

Results given in Table 3 demonstrate that in comparison to healthy participants, the stressful life events reported by breast cancer women are the most unpleasant and their frequency is also high.

Discussion

The study aimed at investigating in women the traumatic life events that may increase the risk of breast cancer which is a major cause of death in women worldwide (WHO, 2009). Numerous researches in west established that 40% of the general population and 20% of the clinicians believe that stress contributes to the risk of breast cancer (Baghurst, Baghurst, & Record, 1992; Steptoe & Wardle, 1994). It was, thus, possible that breast cancer women in the present study may be more prone than the healthy participants to report their stress in an effort to explain their disease. To avoid recall bias, participants were interviewed before diagnosis.

The first hypothesis of the study assumed that higher number of stressful life events by the breast cancer than healthy participants would be reported. The results (Table 2) showed that breast cancer women reported significantly higher number of stressful life events than the healthy participants. These findings suggested the stressful life events as risk factor of breast cancer in women and are in accordance with previous researches which show positive association between stressful life events and breast cancer in women (Cardinalet al., 2008; Duijitset al., 2003; Paleshet al., 2007). The biological explanation of these associations may be stress and stress related hormones (cortisol), which disrupt the functions of various vital systems.

Many aspects of our social, physical, chemical, and biological environmental conditions that foster health also promote the disease. Stressors and the bio-psychosocial response to them involve the brain, endocrine, reproductive, and immune system with short and long terms health consequences. The immediate response to stress as fight or flight can be life-saving, but prolonged and continued stress, especially, when the individual has limited coping skills and resources can be detrimental to health. Numerous mechanisms (independent & interconnected) link the onset and progression of breast cancer with stress. The hypothalamic pituitary adrenal axis involving the hormones, epinephrine, nor-epinephrine, and cortisol are deeply involved in the resilience and vulnerability to stress. The stressful events, when mentally processed, have a strong negative impact on the levels of hormones, neurotransmitters in brain, reproductive and immune system, including antigen presentation, T-cell proliferation, antibody and cell mediated immunity (Franklin, Saab, & Mansuy, 2012; Roberti, Mordoh, & Levy, 2012). As the immune system plays a major role in elimination of cancer cells, impairment in its functions due to prolong exposure to stress and stressful life events increase the risk of cancer and the cancer progression (Tilan & Kitlinska, 2010).

Research suggests that risk of cancer, generally and specifically, the breast cancer increases with adverse life events, higher the number of these events experienced higher is the levels of stress perceived about these events (Brinton et al., 1995; Chenet al., 1995; Kolata, 2005; Lillberget al., 2003, Ollonenet al., 2005). In an early study, Forsen (1991) measured emotional loss and adverse events in the past six years before the onset of cancer among breast cancer women and found increased risk of breast cancer in these women. Cooper and Faragher (1993) on the basis of their findings demonstrated that compared to healthy participants, breast cancer women perceived more severe life experiences. In another study, Chen et al. (1995) rated life experiences of breast cancer patients as severely threatening than the patients with benign breast diseases. The findings of the present study are parallel to earlier research and support our first research hypothesis.

Second hypothesis of the study postulated that breast cancer women would obtain higher life change scores (reflects higher levels of perceived stress) on the SRRS than healthy participants. The data showed significant difference between two groups of women in terms of levels of stress. These results are consistent with previous researches which demonstrated that breast cancer women experience higher levels of stress on account of stressful life events (Cooper &

Faragher, 1993; Eskelinen & Ollonen, 2010; Forsen, 1991; Franklin et al., 2012).

Patticrew, Fraser, and Regan (1999) in a meta-analysis reviewed 29 studies. In the analysis of 12 studies of bereavement as a source of stress, three were positively associated with risk of breast cancer. The analysis of 15 studies which examined other kinds of stress revealed that breast cancer women more than twice than the control group reported stressful life events. The most frequently reported events included divorce or separation, financial problems, and job loss, only two studies found no relationship. In another study, Bower et al. (2014) examined the effect of life time stress on the cancer related fatigue in 50 breast cancer survivors. The result showed that fatigued breast cancer survivors reported higher levels of stress in childhood and adulthood than the no fatigued survivors. Experimental evidence of the increase risk of common cold due to psychological stress has also been reported (Cohen, Tyrell, & Smith, 1991).

Another important finding of the present study is that higher number of breast cancer women than the healthy participants reported death of the close family member, change in health of the family member, death of spouse, death of close friend, change in financial state and divorce and separation as the most frequently occurring adverse events in their past. Some earlier research report similar findings. For example, the meta-analysis by Duijtset al. (2003) death of spouse was found to be significantly associated with increased risk of breast cancer, and in the Cooper and Faragher's (1993) study, higher number of breast cancer than the controls reported death of close friends as the most aversive event.

In the light of the study findings it can be concluded that number of stressful life events (among others) and the amount of stress experienced on account of these events may be a potential risk of breast cancer in women. The findings have implications in the medical field and establish early indicators of stress in breast cancer patients in the cancer trajectory. From practical application, the results have important implications for screening stress and for development of early interventions that may be followed by healthcare professionals to reduce psychological stress in women with breast cancer.

Limitations and Suggestions

The present study has certain potential weaknesses. For instance, the findings of the study are based on sample selected only from one city (Peshawar). Future researchers need to select sample from other

cities as well. The sample of the healthy participants consisting of women having symptoms of breast disease (not diagnosed with breast cancer) is not representative of wider healthy population. It is, therefore, suggested that future researchers should obtain sample of healthy participants from the average population not from women having certain symptoms of breast related problems. In present study, the size of sample was small. Future researchers need to conduct study on large sample. Role of other risk factors such as past history of depression, lack of support available, and certain demographic variables, such as age, education and employment status may be examined in future research.

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