Pre-diagnostic "chronic life stressors" and their association with breast cancer outcomes: A cross-sectional observation study

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ABSTRACT

Background: Breast cancer is widely studied for its psychosomatic aspects owing to its high prevalence among women and the impact of chronic life stressors on its development and outcomes. **Aims and Objectives:** This study aimed to evaluate the association between previous chronic stressors and breast cancer diagnosis, duration of presentation to a health-care facility stage at presentation, tumor profile, treatment compliance, treatment-induced complications, and outcomes. **Materials and Methods:** This cross-sectional observational study included 200 breast cancer patients. Patients were interviewed post-treatment to collect data on marital status, socioeconomic status, occupation, education, and emotional events, using the Holmes and Rahe stress scale. Scores were categorized as low-, medium-, or high-risk for disease development. **Results:** Low-level chronic stress was the most prevalent in patients with stage I disease (93%), followed by stage II (87%), stage III (72%), and stage IV (52%). Moderate-level chronic stress increased with the disease stage, being the lowest in stage I (7%) and the highest in stage IV (48%), and this was significant (P = 0.01). The median duration from symptom recognition to presentation was < 4 weeks in 81–62% of patients with low and moderate stress, respectively. For those with moderate chronic stress, 62% presented within 4 weeks and 38% took > 4 weeks, with a significant P = 0.01. **Conclusion:** Recognizing and addressing pre-diagnostic chronic stress is crucial for breast cancer management because it influences the cancer stage at diagnosis and the time of health-care presentation. Integrating psychosocial support into cancer care can improve treatment effectiveness and patient well-being.

Key words: Breast cancer; Chronic life stressors; Holmes and Rahe stress scale; Cancer outcomes

INTRODUCTION

The influence of psychological factors on disease susceptibility and progression has been a topic of interest since ancient times. Historically, concepts such as "emotional stress" have been used to describe the impact of psychological experiences on health. The modern understanding of this phenomenon is encapsulated by the concept of allostatic overload or bankruptcy, which refers to the physiological wear and tear on the body resulting from chronic exposure to stressors.[1] Breast cancer remains a major global health challenge, with its incidence steadily increasing over the past few decades. Despite advances in early detection and treatment, survival rates and disease progression are not determined solely by biological factors. Psychosocial factors, including chronic stress, have gained recognition as significant contributors to the complexity of breast cancer outcomes.[2,3]

Chronic stress is characterized by sustained exposure to stressors that challenge an individual's coping mechanisms, leading to maladaptive physiological responses.[4] This condition has been linked to various physiological processes that may influence cancer progression, including immune

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system dysregulation, inflammation, and alterations in hormone levels.[5,6] Specifically, stress-related immune suppression can impair the body's ability to combat cancer cells, whereas chronic inflammation can create a tumor-promoting environment.[7] The association between chronic stress and breast cancer outcomes has been supported in numerous studies. Research has shown that high levels of perceived stress are associated with poorer breast cancer prognosis, including more aggressive tumor types and decreased survival rates.[8,9] Furthermore, stress has been linked to reduced adherence to treatment regimens and increased possibility of treatment complications.[4,6]

Despite these associations, the precise nature of how chronic stress influences breast cancer outcomes remains unclear. This observational study aimed to explore the connection between pre-diagnostic chronic life stressors and various aspects of breast cancer outcomes, including tumor characteristics, treatment adherence, complications, and overall treatment effectiveness. The study employed the well-established Holmes and Rahe stress scale[10] to quantify the cumulative stress burden among 200 women diagnosed with breast cancer. By investigating the impact of chronic stressors on breast cancer outcomes, this study sought to provide a comprehensive understanding of the role of psychosocial factors in disease progression and treatment response.

Aims and objectives
This study aimed to evaluate the association between previous chronic stressors and breast cancer diagnosis, duration of presentation to a health-care facility, stage at presentation, tumor profile, treatment compliance, treatment-induced complications, and outcomes.

MATERIALS AND METHODS

This cross-sectional observational study included 200 patients with histologically confirmed breast cancer treated at the Department of Medical Oncology, Government Tirunelveli Medical College, Tamil Nadu, for 6 months from June 2023 to December 2023. This study was approved by the Institutional Ethics Committee before initiation, and informed consent was obtained from all patients.

Inclusion criteria
Patients with histologically proven breast cancer, with either stage I-III disease, who had completed curative treatment and were on follow-up or adjuvant hormonal therapy, and stage IV breast cancer at presentation, who had completed at least 6 months of systemic therapy, were invited consecutively to participate in the study.

Exclusion criteria
Patients who were unwilling to discuss emotional stressors were excluded from the study.

Methods
After receiving medical care, patients were interviewed to gather information on marital status, socioeconomic status, occupation, and education. They also reported emotional events the year before their diagnosis, which were evaluated using the Holmes and Rahe stress scale that measures the stress of life events and their impact on health (Table 1). Patient scores were categorized into low risk (LR), medium risk (MR), and high risk (HR) for disease development based on their total scores. Clinicopathological data collected included TNM stage, histology, grade, blood count, renal and hepatic parameters, chemotherapy regimen and cycles, treatment interruption, neutropenia, and disease status.

Statistical analysis
The data obtained in the interviews were used to evaluate the distribution and relationship of social and clinicopathological parameters with levels of chronic stress before breast cancer diagnosis. Univariate and multivariate analyses were performed to rule out possible confounding factors based on the criteria for each statistical test. For all data, the significance level was set at $P<0.05$. The SPSS 22.0 (Chicago, Illinois, USA) statistical program was used for all analyses.

RESULTS

The median age of the study population was 49.5 years (range: 26–93 years), and all the patients were female. The incidence of LR HRSS (low level of chronic life stressors) was 92%, whereas that of MR HRSS (medium level of chronic life stressors) was 8%; no patient experienced high levels of chronic life stressors. The median duration between the onset of breast cancer symptoms and presentation to the hospital was 6 weeks (range: 1–16 weeks), averaging 3 weeks for patients with low levels of chronic stress and 4 weeks for those with medium levels. The average time to presentation and initiation of treatment (surgery or systemic therapy) was 3 weeks for both low- and medium-stress level patients.

Most patients were married (74%) and had school-level education (57%). Most were unskilled laborers (64%) and belonged to socioeconomic scale IV (81%). The next largest groups were uneducated (39%), unemployed (32%), separated (14%), and socioeconomic scale V (11%) (according to the Kuppuswamy socioeconomic status scale). Smaller percentages included those with a skilled

Table 1: Holmes and Rahe stress scale[10]		
S. No.	Life event	LCU
1	Death of spouse	100
2	Divorce	73
3	Marital separation	65
4	Jail Term	63
5	Death of a close family member	63
6	Personal injury or illness	53
7	Marriage	50
8	Being fired from work	47
9	Reconciliation with spouse	45
10	Retirement	45
11	Change in health of family member	44
12	Pregnancy	40
13	Sexual difficulties	39
14	Addition of family member	39
15	Major business readjustment	39
16	A major change in the financial state	38
17	Death of a close friend	37
18	Changing to different lines of work	36
19	Change in frequency of arguments with spouse	35
20	Mortgage for a loan or major purchase over $ 15,000	31
21	Foreclosure on a mortgage or loan	30
22	A major change in responsibilities at work	29
23	Children leaving home	29
24	Trouble with in-laws	29
25	Outstanding personal achievement	28
26	Spouse begins or stops work	26
27	Starting or ending school	26
28	Change in living conditions	25
29	Revision of personal habits (dress, manners, and associations)	24
30	Trouble with boss	23
31	Change in work hours, conditions	20
32	Change in residence	20
33	Change in school	20
34	Change in recreational activities	19
35	Change in church activities	19
36	Change in social activities	18
37	Mortgage or loan under $15,000	17
38	Change in sleeping habits	16
39	Change in the number of family gatherings	15
40	Change in eating habits	15
41	Vacation	13
42	Christmas	12
43	Minor violation of the law	11

Table 2: Demographic details and clinical characteristics of breast cancer patients	
Characteristics	Percentage
Marital status	
Unmarried	2
Married	74
Separated	14
Legally divorced	2
Widowed	8
Education level	
School level	57
Graduate level	4
Uneducated	39
Occupation	
Skilled occupation	4
Unskilled laborers	64
Unemployed	32
Socioeconomic status	
Scale III	8
Scale IV	81
Scale V	11
Stage at presentation	
I	6
II	22
III	56
IV	16
Hormone receptor status	
HR positive	86
Her2 positives	12
Triple negative	9
HR: High risk	

changes (4%), and other reasons (5%). Moderate-level chronic stress was mostly due to spousal death (74%) or marital separation (63%). Baseline blood parameters were adequate in 64% of the patients, with 36% showing abnormalities, primarily anemia (92%). The predominant chemotherapy regimen was adriamycin/cyclophosphamide (82%), with 6% of patients experiencing treatment interruptions due to cytopenia (Table 3).

Low-level chronic stress was most prevalent in stage I (93%) and decreased with advancing stages, whereas moderate-level stress increased and was highest in stage IV (48%). The comparison between the disease stage and stress levels was significant (P=0.01). The median presentation time was <4 weeks for 81% of low-stress patients and 62% of moderate-stress patients, with a significant difference (P=0.01) (Table 4).

DISCUSSION

In this study, we investigated the association between pre-diagnostic chronic life stressors and breast cancer outcomes. Our findings revealed that most participants (92%) experienced low levels of chronic stress, whereas only 8% had medium levels of stress. Participants reported no high levels of chronic stress. The study population exhibited a

occupation (4%), graduate education (4%), unmarried status (2%), and legally divorced status (2%). The patients were diagnosed with stage III breast cancer (56%) and the majority had HR-positive disease (86%). Stages I and II were less common (6% and 22%, respectively), and 16% of patients had stage IV disease, with 2 positivity in 12% and 9% of patients, respectively (Table 2).

Among these patients, 16% had stage IV disease, with an 8% complete response rate, 72% partial response, 10% stable disease, and 10% progressive disease rate. Low-level chronic stress was primarily caused by changes in the health of family members (64%), followed by major financial changes (18%), trouble with in-laws (9%), spousal work

Table 3: Disease and stress-related factors in breast cancer patients

Factors	Percentage
Disease	
Stage IV	16
Complete response	8
Partial response	72
Stable disease	10
progressive disease	10
Life events leading to low-level chronic stress	
Change in health of family member (LCU-44)	64
The major change in financial state (LCU-38)	18
Trouble with in-laws (LCU-29)	9
Spouse begins or stops work (LCU-26)	4
Others	5
Life events leading to low-level chronic stress	
Death of a spouse (LCU-100)	74
Marital separation (LCU-65)	63
Baseline blood parameters	
Adequate CBC, RFT, and LFT	64
Abnormal baseline blood parameters	36
Anemia (secondary to iron deficiency)	92
Chemotherapy regimens	
Adriamycin/cyclophosphamide	82
FEC, FAC, TCH, and TAC	18
Treatment interruption	
>Week (due to cytopenia)	6

Table 4: Comparison of cancer stages and presentation times between chronic stress levels

Stage	Low-level chronic stress (%)	Moderate-level chronic stress (%)	P-value
Cancer stages			
I	93	7	0.01
II	87	13	
III	72	28	
IV	52	48	
Presentation time (weeks)			
<4	81	62	
>4	19	38	

range of disease stages at presentation, with the majority presenting stage III. The average time from symptom onset to hospital presentation was relatively short, and treatment initiation occurred promptly, regardless of stress levels. The most common life events contributing to low and moderate levels of chronic stress were significant changes in family health and the death of a spouse, respectively.

Pre-diagnostic stress and disease stage

Previous studies have indicated that chronic stress is associated with advanced stages of the disease at diagnosis. Lutgendorf et al., (2010) found that higher levels of stress were linked to a greater of presenting with advanced breast cancer. Our study's finding that a significant proportion of patients presented at stage III aligns with this literature, suggesting that while stress might influence disease progression, other factors also play a critical role.[3]

The impact of stress on symptom recognition and presentation

The findings by Bower et al., observed that patients with moderate chronic stress had a longer median duration from symptom onset to presentation compared to those with low stress.[6] This supports the view that stress may delay help-seeking behaviors, potentially due to exacerbated psychological distress and impaired health awareness Antoni et al. However, the difference in time to presentation was statistically significant only for patients with moderate stress, indicating a possible threshold effect.[5]

Treatment compliance and outcomes

Our results showed no significant differences in treatment compliance or outcomes based on stress levels. This finding suggests that chronic stress adversely affects treatment adherence and response. Thaker and Sood[9] and Dutton et al.,[11] reported that high stress levels are associated with poorer treatment adherence and reduced efficacy. In our study, treatment interruption was minimal and predominantly due to cytopenias, suggesting that stress may not have had a substantial impact on treatment regimens or adherence.

Socioeconomic and demographic factors

The socioeconomic and demographic characteristics of the study population, including low education levels and high unemployment rates, are consistent with findings in other studies, such as those by Gonzalez and Sharp[12] and Dalton et al.[13] (2008), which highlighted the influence of socioeconomic factors on cancer outcomes. The predominance of low socioeconomic status in our study underscores the need for targeted interventions addressing both psychosocial and economic aspects.

Life events and stress levels

The life events identified in our study are consistent with previous research on stressors affecting patients with cancer. The death of a spouse and significant financial changes have been identified as major stressors in other studies such as Holmes and Rahe, Stommel and Kurtz. The high incidence of these stressors among patients with moderate stress levels reinforces the importance of considering specific life events when evaluating the impact of stress on cancer outcomes.[14]

Clinical implications

Our findings suggest that while pre-diagnostic chronic stress is prevalent among patients with breast cancer, its impact on disease stage at presentation and treatment outcomes may be moderated by other factors. The high incidence of low-stress levels among participants could indicate effective stress management strategies or a lower perceived impact of stress. However, moderate stress

was associated with a longer time to presentation, which emphasizes the need for early psychological support to improve promptness in seeking medical care.

Limitations of the study

The limitations of this study include its observational nature and the absence of multivariate analysis, which might have provided a deeper understanding of the interplay between stress and other variables. In addition, reliance on self-reported stress measures may introduce bias. Future research should consider longitudinal studies with larger and more diverse populations to further elucidate the relationship between chronic stress and breast cancer outcomes. The inclusion of qualitative assessments of stressors and exploration of intervention strategies can provide valuable insights.

CONCLUSION

Our study underscores the importance of recognizing and addressing pre-diagnostic chronic life stressors in the management of breast cancer. The observed associations between chronic stress levels, cancer stage at diagnosis, and time to presentation to health-care professionals highlight the need for comprehensive psychosocial assessments and interventions as part of cancer care protocols. Further research is warranted to elucidate the underlying mechanisms driving the observed associations and explore the effectiveness of targeted interventions aimed at mitigating the adverse effects of chronic stress on breast cancer outcomes. By integrating psychosocial support into cancer care pathways, we can strive to optimize treatment effectiveness, improve patient well-being, and enhance the overall quality of care for individuals undergoing breast cancer diagnosis and treatment.

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