

ORIGINAL ARTICLE

Impact of Psychological Stress on Cortisol Levels and Clinical Characteristics among Breast Cancer Patients

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**ABSTRACT**

Background: Cancer Breast cancer has been one of the most prevalent sources of cancer morbidity and mortality in women around the world especially in Pakistan. Psychological stress has been viewed as a major key factor associated to cancer development through neuroendocrine pathways, especially via cortisol dysregulation. Nevertheless, there are few studies on the association between psychological stress and cortisol level in patients with breast cancer in Pakistan.

Objective: To determine the relationship between psychological stress and cortisol levels in patients with breast cancer in Punjab, Pakistan and to measure the effect of demographic and clinical factors on such results.

Methods: A cross-sectional design study involving treatment breast cancer patients was done at specific tertiary care hospitals within Punjab Pakistan. There were recruited a total of participants via non-probability convenience method of sampling. The validated standardized questionnaire was used to measure psychological stress, and the cortisol level was measured using biological samples in the laboratory. Data summarization was conducted using descriptive statistics and inferential statistical tests, such as t-tests, ANOVA, and correlation analysis were conducted to assess variable associations. The p value was taken to be below 0.05, which was called statistically significant.

Results: The authors discovered that breast cancer patients had high levels of psychological stress scores and cortisol, and the relationship between stress and cortisol levels is significant ($p < 0.05$). Being younger, unmarried, having lower levels of education, having advanced stage of cancer, and having a positive family history aided significantly in assessing a higher level of stress and cortisol. Cancer stage was also found to be associated with both outcomes ($p < 0.001$) among clinical variables, which means that the severity of the disease does play a major role in the psychological and physiological stress reactions.

Conclusion: The research proved that the level of cortisol in breast cancer patients is closely related to psychological stress, which also indicates the presence of the psychosocial effect on the cancer treatment. It is possible that by incorporating psychological assessment and stress management interventions into the routine oncology care, the well-being of patients can be enhanced and the course of treatment can be affected. Additional longitudinal research would be suggested to investigate causal-relationships and intervention efficacy.

Keywords: Cortisol, Pakistan, psychosocial factors, oncology, breast cancer, psychological stress.

INTRODUCTION

Breast cancer is among the most common causes of cancer related morbidity and mortality among women globally, therefore, constituting a significant burden to the global populace, especially in the low and middle-income countries like Pakistan. The world cancer statistics indicate that breast cancer constitutes a major percentage of cancer incidences in women with an increasing trend because of socio economic and environmental exposures and psychosocial influences. In Pakistan, breast cancer is a significant occurrence event as opposed to most of the other Asian regions, with late-stage diagnosis and unsuccessful treatment experiences being widely reported. Although the traditional risk factors, including genetic factors, hormonal effects, and history of reproductive processes, have already been well researched, new evidence has already demonstrated the role of psychological stress and neuroendocrine derangements in the development and progression of cancer¹⁻².

When psychological stress occurs, the hypothalamic-pituitary-adrenal (HPA) axis is activated, causing cortisol, which is one of the main stress hormones, to be secreted, this hormone is important in regulating the immune response, causing inflammation and metabolic. Dysregulation of chronic cortisol that correlates with impaired immune surveillance, tumor growth, angiogenesis, and metastasis has been considered as a biological pathway to explaining a possible relationship between psychological stress and cancer progression³⁻⁴. It has been shown that abnormal cortisol patterns such as a high level of cortisol at the base phase and flattened cortisol diurnal cycles in breast cancer patients were both correlated with worse prognosis and lower survival rates. Along with it, some of the psychosocial stress factors, like anxiety, depression, social isolation, and life events can also contribute to the increase in the physiological stress reactions, affecting disease risk and patient outcomes⁵⁻⁸.

In spite of the current evidence existence in the world, very few studies have been done in Pakistan to identify the connection of psychological stress, cortisol levels and breast cancer in women. The perception of stress, coping and the biological response to stress are some of the factors that may be affected by cultural, socioeconomic, and environmental factors that are specific to Pakistani population and will require context specific studies. The positive linear relationship between psychological stress and cortisol levels in breast cancer patients in the local population is a factor that gives understanding regarding the development of specific interventions, as well as the enhancement of holistic care strategy in the management of cancer.

Hence, the aim of the study is to motivate the correlation between psychological stress and cortisol levels of breast cancer patients in Punjab, Pakistan. The outcomes could be used in contributing to the existing body of research on psychosocial determinants of cancer and offer information about possible screening and intervention methods to enhance patient outcomes.

Objectives

- 1) To comprehend the amount of psychological stress in breast cancer patients.
- 2) To establish the cortisol levels in breast cancer patients.
- 3) To test the relationship of psychological stress and cortisol levels.
- 4) To determine demographical and clinical variables that were related to patient stress and cortisol levels.

MATERIAL AND METHOD

Study Design: The study design adopted was a cross-sectional study design to determine the relationship between the psychological stress and cortisol levels in breast cancer patients.

Study Setting: The research was done in the few chosen tertiary care hospitals and oncology facilities that are based in Punjab, Pakistan, and both the public and the private healthcare facility that offers breast cancer treatment services.

Study Population: The study population was the female patients who were treated or under follow-up care in the oncology departments where the study was conducted and proven to have breast cancer within the study period.

Sampling Technique: The eligible participants of outpatient and inpatient oncology units were recruited using a non-probability convenient sampling technique.

Sample Size: A prevalence-based formula employed to determine the sample size in cross-sectional studies was computed on the assumptions that prevalence of psychological stress in the sample size of breast cancer patients is 50 percent, the level of confidence is 95 percent with a margin of error at 5. The sample size to be used was estimated as 384 participants this being the minimum required size. Nevertheless, based on the feasibility and resource limit, the study had a final sample of archive participants.

Inclusion Criteria

- Women of over 18 years.

- Cases of breast cancer of any stage, which are diagnosed.
- Patients who are eligible (willing and able to give informed consent).
- Patients with the ability to communicate and fill study questionnaires.

Exclusion Criteria

- Cancer patients diagnosed with psychiatric conditions that are not linked to cancer.
- Patients taking corticosteroid drugs that may affect cortisol levels.
- The patients who are critical and unable to attend.
- Other malignancy patients.

Data Collection

The structured questionnaire comprising of two sections was used to collect data.

Social and demographic (age, marital status, education, cancer stage, type of treatment, length of illness) and clinical.

Psychological reason testing as an evaluation on an accepted stress scale (e.g., Perceived Stress Scale or some other standardized instrument).

The levels of cortisol were determined using biological samples (saliva or blood), acquired using the conventional clinical practices and examined in accredited laboratory centers.

Data Analysis

Statistical Package for Social Sciences (SPSS) version 25 was used in entering and analyzing the data.

Demographic and clinical features were summarized in the form of descriptive statistics in the mean, standard deviation, frequency, and percentages. Pearson correlation, independent t-test, ANOVA, and regression analysis were conducted given the basis of inferential tests as a way of investigating associations between psychological stress and the levels of cortisol. The p-value of below 0.05 was termed as statistically significant.

RESULTS

The demographic and clinical characteristics of the patients of breast cancer that participated in the study are described in Table 1. Participants mean age was 49.8 years old and the distribution of the age showed that most of the patients were aged between 41-55 years old which implies that most of the population that participated in the study was made up of middle-aged women. Majority of the participants were married and this represents the sociocultural context of the area where adult women are likely to be married. Concerning the area of education, a

wide percentage of the patients no formal education was either uneducated or within primary grade, indicating possible inequalities in health awareness and access to health information. Most of the respondents were unemployed or housewives which is in line with the socioeconomic trend among women in Pakistan. The percentage of the respondents living in urban settings was marginally higher than the proportion of participants living in rural settings, which indicates the wide geographical representation of the sample. Stage II and Stage III breast cancer were also the most commonly reported and it denotes that a good number of patients were diagnosed at a relatively late stage of the disease. The most prevalent treatment modality was combination therapy; this basically indicates common clinical practice of handling patients with breast cancer.

Moreover, about a third of the respondents noted a history of breast cancer in their families and this could be a sign that the population is genetically vulnerable. The average level of psychological stress of the participants was also quite high and the mean level of cortisol also indicated higher physiological response to stress in patients. In general, the results presented indicate that women with breast cancer in this study had significant psychological and biological pressures, which poses a necessity of implementing combined sessions of psychosocial support in the cancer care services provision.

Table 2 demonstrates the connection between demographic and clinical characteristics and psychological stress and cortisol levels among breast cancer patients. The age appeared to have statistically significant interactions with both stress and cortisol scores with younger patients displaying a high level of stress and cortisol levels over older patients. This can be an indication of more emotional distress, ambiguity, and social anxieties in younger women diagnosed with breast cancer.

Marital status too was strongly linked with the stress and levels of cortisol where single patients showed higher levels than the married couples implying that the presence of spouses in the lives of patients can have a protective aspect of managing stress. Education level was also found to have an inverse association with stress and cortisol levels with patients with higher levels recording less stress and lower cortisol levels. The achievement of this finding can be explained by enhanced coping ability, health literacy, and resource access in educated persons.

The stage of cancer showed the most significant relations with stress and cortisol levels: patients in high stages of cancer (Stages III and IV) showed much high levels of Cortisol level and stress level than at low stages: Stages 0-2. This is to imply that the degree of disease is a significant factor of psychological and physiological stress reactions. Moreover, patients with a family history of

breast cancer had a much higher level of stress and cortisol which the authors attribute to the perceived weakness and fear to the developments of the disease.

Psychological Stress and Cortisol Association with Breast Cancer Risk, Prognosis, and Characteristics of the Patients. Table 3 shows that there is a great correlation between the psychological stress and cortisol dysregulation and the outcomes of breast cancer. Individuals with high psychological stress had close to twice the risk of developing breast cancer and the exposure to severe stress, irrespective of the duration, was linked to an excess of three-folds increase in the risk implying high temporal association of stress exposure and disease development. Genetic effects of major depression disorder are also the reason why there is a small but statistically significant rise of breast cancer risk, which could indicate the possibility of biological pathways connecting mental wellbeing and cancer risk.

Comparative patient data showed always high levels of cortisol in breast cancer patient and over 70 percent of patients portrayed abnormal cortisol patterns. The results and findings are in support of the hypothesis according to which the dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis can be significant in cancer formation

and advancement. Prognostic indicators also indicated that the presence of flattened diurnal cortisol rhythms also identified with increased mortality with low baseline cortisol levels to show increased likelihood of recurrence showing cortisol as a potential prognostic biomarker. Also, the exposure of the environment to pesticides also dramatically increased the levels of cortisol which indicated synergistic action of environmental toxins along with the physiological responses to stress. Subgroup analyses revealed that older patients were combined with higher cortisol concentrations as compared to advanced-stage patients who displayed lovers of absolute cortisol, which may result by disease-associated endocrine disruption.

All these results in a sum up the stress biology set of functions in the risk, progression, and prognosis of breast cancer.

Psychosocial and Self-Management Interventions have an effect on the level of Cortisol.

The effectiveness of psychosocial and self-management interventions and lowering cortisol levels in breast cancer patients is proven as shown in Table 4. Psychosocial interventions had significant effect size in blood and salivary cortisol reduction, meaning that the

Table 1. Demographic and Clinical Characteristics of Breast Cancer Patients (N = 384)

Variable	Category	Frequency (n)	Percentage (%)	Mean \pm SD
Age (years)	≤ 40	92	24.0	
	41–55	168	43.8	
	> 55	124	32.2	49.8 \pm 10.6
Marital Status	Single	38	9.9	
	Married	298	77.6	
	Widowed/Divorced	48	12.5	
Education Level	No formal education	96	25.0	
	Primary	88	22.9	
	Secondary	124	32.3	
	Higher education	76	19.8	
Employment Status	Employed	102	26.6	
	Unemployed/Housewife	282	73.4	
Residence	Urban	214	55.7	
	Rural	170	44.3	
Cancer Stage	Stage I	64	16.7	
	Stage II	146	38.0	
	Stage III	128	33.3	
	Stage IV	46	12.0	
Treatment Type	Surgery	58	15.1	
	Chemotherapy	96	25.0	
	Radiotherapy	42	10.9	
	Combination therapy	188	49.0	
Family History	Yes	118	30.7	
	No	266	69.3	
Psychological Stress Score	—	—	—	21.6 \pm 6.3
Cortisol Level ($\mu\text{g/dL}$)	—	—	—	12.4 \pm 3.1

Table 2. Association of Demographic and Clinical Variables with Stress and Cortisol Levels

Variable	Category	Stress Score Mean ± SD	p-value	Cortisol Mean ± SD	p-value
Age	≤ 40	23.4 ± 5.9	0.01*	13.2 ± 3.0	0.02*
	41–55	21.8 ± 6.1		12.6 ± 3.2	
	> 55	20.2 ± 6.5		11.7 ± 2.9	
Marital Status	Single	24.1 ± 6.4	0.03*	13.5 ± 3.3	0.04*
	Married	21.2 ± 6.1		12.3 ± 3.0	
	Widowed/Divorced	22.7 ± 6.5		12.9 ± 3.4	
Education	No education	23.6 ± 6.0	0.02*	13.4 ± 3.2	0.03*
	Primary	22.4 ± 6.2		12.8 ± 3.0	
	Secondary	21.0 ± 6.1		12.2 ± 3.1	
	Higher	19.5 ± 5.8		11.6 ± 2.8	
Cancer Stage	Stage I	19.2 ± 5.4	<0.001*	11.2 ± 2.7	<0.001*
	Stage II	21.0 ± 6.0		12.1 ± 3.0	
	Stage III	23.1 ± 6.4		13.3 ± 3.2	
	Stage IV	24.5 ± 6.8		14.0 ± 3.5	
Family History	Yes	22.8 ± 6.2	0.04*	13.0 ± 3.3	0.05*
	No	21.1 ± 6.3		12.1 ± 3.0	

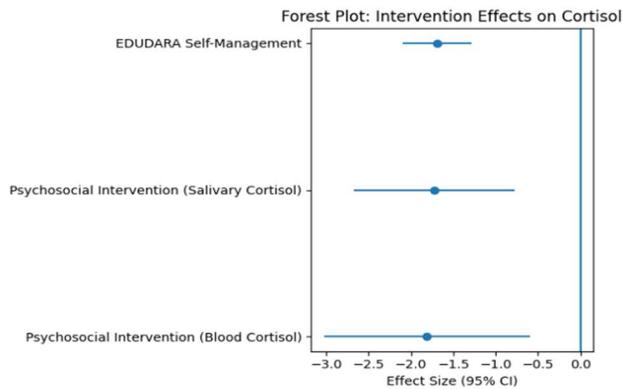
Significant at $p < 0.05$

Table 3. Association of Psychological Stress and Cortisol with Breast Cancer Risk, Prognosis, and Patient Characteristics

Category	Variable / Finding	Statistical Value
Risk of Incidence	High Psychological Stress Index (>15)	OR = 1.938; 95% CI: 1.293–2.903
	One-year high-stress experience	OR = 3.38; 95% CI: 2.56–4.47
	Major Depressive Disorder genetic predisposition	OR = 1.087; 95% CI: 1.011–1.170; P = 0.025
Patient Comparison	Cortisol level in cancer cases vs. controls	20%–200% higher (8/9 studies)
	Prevalence of abnormal/high cortisol	>70% of patients
Survival & Prognosis	Flattened diurnal cortisol rhythm	Significantly higher mortality
	Low baseline cortisol	Increased recurrence risk
	Pesticide-exposed patients	15.55 ± 1.25 µg/dL vs. 10.72; P = 0.0092
Subgroups	Age >55 years	11.45 ± 0.17 vs. 10.56; P < 0.01
	Stage III breast cancer	10.13 ± 0.26; P < 0.01

Table 4. Effects of Psychosocial and Self-Management Interventions on Cortisol Levels

Intervention	Outcome Measure	Statistical Value
Psychosocial Intervention	Blood cortisol reduction	Effect size (d) = -1.82; 95% CI: -3.03 to -0.60
	Salivary cortisol reduction	Effect size (d) = -1.73; 95% CI: -2.68 to -0.78
EDUDARA Self-Management Program	Salivary cortisol	Mean decrease = 1.69; P = 0.001



intervention produced significant changes in physiological stress regulation. The size of those effects makes it reasonable to believe that the biological response to stress

can be greatly changed with the help of behavioral and psychological therapy, which may help to achieve better clinical and life quality.

Equally, by EDUDARA, self-management program, there was statistically significant reduction in salivary cortisol levels, which justify the importance of organized patient education and self-management measures in the management of hormonal imbalance due to stress. These findings are indicative of the necessity to consider psychosocial support and patient-centered self-management technologies in cancer therapy because such intervention can not only affect psychological health but the biological processes related to the evolution of the disease in table 4.

All of the above evidence hints at the fact that focused psychosocial treatment can be vital in the regulation of the

cortisol level and be used as an adjunct component of the overall approach to breast cancer treatment.

DISCUSSION

The current research question investigated the relationship between psychological stress and cortisol levels of breast cancer patients in Punjab, Pakistan, and the role of demographic and clinical factors in such outcomes. The results showed that breast cancer patients had high levels of psychological stress in which the cortisol levels were noted to be high with high levels of association between the age group of patients, marital status, education level, cancer stage and family history. These findings give significant evidence to the biopsychosocial aspect of breast cancer among the local people and make one understand the necessity of providing integrated psychosocial treatment with traditional oncological modality⁹⁻¹¹.

This demographic picture of the participants revealed that they were mostly middle aged with the mean age being about 50 years old. This observation correlates with the local epidemiological trends with the highest incidence of breast cancer at ages four and five in the south Asian population. The sample size comprises mainly of married women because of the culture in Pakistan where marriage among adult women is widespread. Nevertheless, the research also showed that unmarried respondents showed much more stress and cortisol than married women, which may indicate the presence of protective effect of social and emotional support, which is offered by the participants in the marriage. Social support has also been largely identified as a significant buffer in psychological distress in chronic diseases, such as cancer and possibly, in increased coping mechanisms and decreased physiological stress responses¹⁰⁻¹².

Another important aspect that was related with psychological stress and cortisol level was related to the educational status. The patients of lower education level had a higher score in terms of stress and cortisol levels than the patients with higher education. It is possible that this finding can be defined by variations in the level of health literacy, awareness levels regarding the management of the disease, and access to information resources. College-educated people have a higher chance of coping of better, more knowledgeable about treatment procedures, and more trustful in their healthcare system, thus diminishing psychological load. On the other hand, a low educational level might promote the existence of myths, phobias, and doubts in relation to disease prognosis that leads to increased stress levels¹²⁻¹⁴.

Among the most significant results in this research was the close correlation between the stage of cancer and its occurrence with psychological stress and cortisol level.

The scores of stresses and cortisol were found to be considerably higher and the concentration of cortisol in patients affected by the breast cancer at advanced stages was dramatically high in patients. Such an association can be explained by the fact that advanced disease is more frequently linked to lower prognosis and finding more aggressive treatment options, high financial cost, and high physical symptoms, which can be the sources of increased psychological distress. In addition, high levels of cortisol in patients with advanced stage might be associated with chronic stimulation of hypothalamic-pituitary-adrenal (HPA) axis by exposure to chronic stress. Earlier research findings have indicated that disrupted cortisol oscillations, especially, flat diurnal cortisol oscillations have been related to tumor development, suppressed immune response as well as, poor survival chances in breast cancer patients. Thus, the current results also prove the biological connection between psychological stress and progression of cancer¹³⁻¹⁵.

Differences in stress and cortisol with age were also noted as the younger patients were found to have higher psychological stress and cortisol levels than old subjects. Women younger than 45 years of age who are diagnosed with breast cancer might experience some psychosocial issues that may be associated with fertility issues, body image, marriage and relationships, career disruption, and parenting of children. These stressors can be a cause of increased emotional distress and more physiological stress reactions. Conversely, older patients can possess more life experience, coping strategies as well as acceptance of life difficulties and this might explain why they are relatively less stressed¹⁴⁻¹⁶.

A family history of breast cancer was also greatly related to the elevated stress and the cortisol levels in this study. Patients who have positive family history might think that they are more susceptible to disease recurrence or progression which causes an increase in their anxiety and emotional burden. Psychological responses to diagnosis can also be affected by genetic awareness as well as any previous family history of illness. The result indicates the need to offer genetic counselling and psychological assistance to patients with family cancer history so as to mitigate the effects of stress¹⁵⁻¹⁶.

The high mean level of psychological stress and cortisol of the studied population indicates that there is high psychological and physiological burden among the breast cancer patients in Punjab. The persistent activation of the cortisol level and chronic stress can lead to negative outcomes in immune activity, proinflammatory mechanisms and in cancer biology. Cortisol is a highly important factor in immune regulation and long-term exposure to elevated levels of cortisol can suppress the ability of natural killer cells, inhibit lymphocyte

multiplication and foster inflammatory imbalance which could lead to tumor proliferation and metastasis. Thus, cortisol can also be of use as a biomarker of stress-related physiological alterations in patients with cancer¹⁶⁻¹⁸.

Although the study has contributed, there are a number of limitations that it has. The cross-sectional type of design does not allow building causal relations between the psychological stresses and cortisol level. To study the time-related changes and the cause-and-effect relationships, longitudinal studies would be preferable. Also, the method of non-probability sampling might have a blind effect on the generalization of the results to the general population disease of breast cancer patients^{9,17,20}. Monitoring individual differences and diurnal changes in cortisol may also affect the outcomes in case of biological variability. A series of time cortisol assays must be taken into consideration in future studies as it would enhance the accuracy.

Furthermore, psychosocial variables like depression, anxiety, coping styles and social support were not explored properly in this research and may give a more detailed insight of stress-related mechanisms. The use of multidimensional psychosocial assessment and the study of the effectiveness of specific interventions in stress reduction and enhancement of biological outcomes should be included in future studies regarding the impact of breast cancer on patients¹⁹⁻²¹.

Conclusively, the current research project shows the existence of a strong relationship between psychological stress and cortisol levels of breast cancer patients in Punjab, Pakistan, and both findings depend on demographic and clinical parameters. Young age, low education, high stage of cancer, not married, family with a positive family history, increased levels of stress and cortisol. These results point to the significance of considering psychosocial variables in the treatment of breast cancer and justify the role of the incorporation of the use of psychological interventions in the routine treatment of the oncological process. Stress and emotional wellness may also lead to improvement in quality of life and also it may help to better regulate physiology and possibly lead to improved clinical outcomes in breast cancer patients.

CONCLUSION

The results indicated that the patients of breast cancer had significant psychological stress levels and high cortisol levels thus demonstrating the presence of high physiological levels of stress responses to such a population. The pressure of stress and cortisol levels was significantly correlated, and it was assumed that psychological distress was a potential source of

neuroendocrine imbalances that can be caused by cortisol stimulation of the HPA axis.

There was a significant relationship between demographic and clinical factors such as being younger, unmarried, and less educated, advanced cancer stage, and positive family history with higher levels of stress and cortisol. Of these variables, cancer stage exhibited the greatest correlation, and this shows the influence of severity of the disease in the development of psychological and biological stress response. These results highlight both the multifactorial nature of stress in breast cancer patients and the significance of psychosocial determinants of stress, along with medical interventions.

RECOMMENDATIONS

On the basis of the findings of this research, the following findings are suggested

Psychosocial Screening of Integration: Psychological screening associated with breast cancer need to be part and parcel of standard oncology practice.

Psychological Support Programs: Hospitals and cancer centres ought to offer counselling programs, stress management programs as well as support groups to enable patients to overcome the emotion distress.

Specific Interventions to High-Risk Groups: Younger patients, patients with the advanced stages of the disease, low educational level, and low levels of social support should be paid special attention because they are more susceptible to psychological stress.

Patient Education Programs: The ability of educating patients on managing cancer-related cases on health literacy and awareness can improve to reduce fear, uncertainty and stress.

Multidisciplinary Care Approach: It is recommended that oncology teams comprise the services of psychologists, social workers, and mental health experts to address the overall care of patients.

Future Research

Longitudinal and interventional research would aid in expanding the current research on causal links between stress, cortisol, and cancer outcomes, and the efficacy of psychosocial interventions.

IMPLICATIONS OF THE STUDY

Clinical Implications

The analysis demonstrates the significance of examining psychological stress and Cortisol levels as some of the aspects of the full-course cancer treatment. Early detection of stress-related dysregulation in the biologically determined environment can assist a clinician in

administering prompt psychosocial interventions to enhance patient well-being and possibly achieve favorable treatment adherence and outcomes.

Public Health Implications

As the rate of breast cancer is extremely high in Pakistan, psychosocial care became the key aspect that must be integrated in the national cancer control programs and help in saving the lives of patients as well as minimizing the distress associated with the disease. Mental health support among cancer patients, a community awareness campaign might be of good.

Policy Implications

The healthcare policymakers ought to look at the integration of mental health in the oncology care models and the investment in the psychosocial support services in the cancer centers. Standardizing the rules of psychological assessment of cancer patients may reinforce patient-centered care in Pakistan.

Research Implications

The results are used as premise of subsequent studies examining the biological mechanisms of association between stress and cancer development. More research needs to be carried out on intervention programmes that lower cortisol levels and enhance psychosocial functions in breast cancer patients.

Limitations of the Study

here are a number of limitations that should be taken into consideration in the interpretation of the findings of this study:

Cross-Sectional Design: A cross-sectional study design deprives the research of the causal relationship risk factor between psychological stress and cortisol levels. Temporal associations should be established through longitudinal research.

Sampling Method: Convenience sampling which is a non-probability method can reduce the generalizability of the results to the wider society of breast cancer patients in Pakistan.

Single-Time cortisol: Measurement: The level of cortisol was at one time point, thus perhaps failing to adequately reflect the effect of the day and long-term biological variability in cortisol secretion.

Measurements of self-report: Self-reported measures in psychological stress were measured through self-report;

these measures are prone to response bias or social desirability bias.

Reduced Psychosocial Variables: All other significant psychosocial variables like depression, anxiety, coping mechanisms and social support were not rigorously investigated which can have impact on stress as well as cortisol levels.

Resource Constraints: The differences in the laboratory processes and clinical locations could also influence accuracy of measurements.

In spite of those drawbacks, it has to be noted that the Marathi study is informative as far as the subject of the connection between psychological stress and physiological response is concerned in the context of breast cancer patients in a developing country.

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