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Original Research Article

Impact of Stress on the Immune System in Cancer Patients

Arun Kumar Singh[1], Kumar Nitin[2]

[1]Associate Professor, Department of Medicine, Rohilkhand Medical College, Bareilly, Uttar Pradesh, India

[2]Assistant Professor, Department of Medicine, Rohilkhand Medical College, Bareilly, Uttar Pradesh, India

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Corresponding Author: Dr. Kumar Nitin

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Abstract

Background: Strong evidence indicates that stress has a significant negative effect on people's health, primarily by disrupting the immune system's normal functioning and causing a low-chronic inflammatory state that increases the risk of infections, metabolic disorders, and other illnesses. The current study intends to assess the stress levels of some patients being treated in an anti-cancer facility and look for any potential links to their immune system status before implementing a physical/psychological programme to prevent health deterioration.

Methods: From a psychological and immunological standpoint, we investigated 50 patients and looked at neutrophil chemotaxis and phagocytosis, lymphocyte chemotaxis and proliferation, and natural killer (NK) cell activity in particular.

Results: Women were shown to have greater depression symptoms than men. Chemotaxis levels of lymphocytes and neutrophils in women were much lower than in men. We also discovered a strong inverse relationship between depression and NK cell activity. This association was strong regardless of gender.

Conclusion: We conclude that stress has an effect on NK activity, and we propose that a combined treatment of cognitive behavioural therapy and physical activity programmes may ameliorate patient health deterioration.

Keywords: Stress, Chemotaxis, Neutrophil, Lymphocyte, Natural Killer (NK) Cell,

Introduction

Clinically, Psychoneuroimmunology (PNI) encompasses the understanding of immunological responses created in psychiatric diseases as well as the knowledge of biological mechanisms subordinated to underlying psychosocial events that initiate and/or develop the immunological disease. Evidence suggests that the neural and immunological systems interact. Several studies in humans have found that depression or stressors such as bereavement, divorce, a demanding work environment, or students during exam periods cause a decrease in NK, neutrophil, and lymphocyte activities such as lysis, proliferation, and chemotaxis, making these immune cell activities good markers of immune status in patients [1-3].

Stress also alter the synthesis of hormones such as adrenaline, corticoids, and catecholamine, all of which have an impact on the immune system (Leonard, 2010).[4] Stress, depression, and inflammation have all been shown to trigger and affect cytokine homeostasis (Kiecolt-Glaser et al., 2003).[5] Cytokines may have a depressive effect directly by producing corticotrophin or indirectly by increasing resistance to glucocorticoid receptor activation. As a result of the suppression of the HPA axis's natural feedback mechanism, the system will become hyper-activated.

Lymphocyte Chemotaxis Index (LCI), Neutrophil Chemotaxis Index (NCI), Neutrophil Phagocytic Index (NPI), lymphocyte proliferation (LP), and NK activity (NK lysis%) are all common markers used to assess immune function. Previous research has demonstrated that immune biomarkers are altered in response to stress (Khanfer et al., 2010; Vitlic et al., 2014; Duggal et al., 2015, 2016).[6-9] Thus, chronic stress decreases chemotaxis of mononuclear cells in peripheral blood (Redwine et al., 2004),[10] and phagocytic activity of neutrophils (PAN) has been reported downregulated in clinically depressed patients as well as LP and NK activity (Gan et al., 2002; McGuire et al., 2002).[11-12]

With the physical and mental trauma of cancer, more people prefer to obtain a specific therapy aimed at reducing the symptoms of stress in order to improve their quality of life. We also feel that a psychological/physical programme aimed at preventing physical and physiological degeneration could accomplish this. However, before implementing this programme, it would be required to understand each

patient's stress levels, as well as his or her immunological health. Thus, we attempted to characterise immunological state in a cancer group that is frequently stressed. We also wanted to see if the patient's gender, given the psychological and physiological differences between men and women, would influence these assessments. Thus, the goal of this study was to see if there was a link between stress status in patients being studied in cancer unit and immune response markers in these patients prior to implementing a physical activity programme to prevent physical and psychological deterioration.

Materials and Methods

This study was conducted after taking approval from Institutional Ethics Committee and consent from the patients who were willing to participate in the study. A well informed written consent was taken prior to the study.

We investigated the immune system status of 50 patients (28 women and 22 men) from the Spanish middle-upper class who developed their professional lives under stressful situations. Following a psyche-clinical evaluation, the patients were tested in an antiaging unit to ascertain their baseline biological age from both a physical and psychological standpoint.

This investigation was conducted in our institution's antiaging centre. In a nutshell, the antiaging unit concentrated on giving psychological and medical care to patients who sought to avoid physical and cognitive decline. The patients were evaluated from both a medical and psychological standpoint, and they received a report in which the medical-psychological team decided on a treatment plan that included pharmacological and psychological therapy, as well as physical activity and nutritional suggestions.

Between 8 and 10 a.m., blood samples were drawn from an inner fold arm vein using VacutainerR tubes under fasting circumstances. One tube of 5 ml (containing separating gel and clot activator) was taken from each subject for serum hormone levels. Two tubes of 10 ml (sodium heparin) were collected each patient for immune cell functional assays such as lymphocyte proliferation, neutrophil phagocytic, lymphocyte/neutrophil migration, and NK activity assays.

We measured the levels of sexual hormones (progesterone, testosterone, estradiol 17, and prolactin), thyroid hormones (TSH and T4), insulin, and insulin-like growth factor I (IGF-I) in the patients' blood samples.

In particular, we examined neutrophil function, chemotaxis index (NCI), and phagocytosis index (NPI); lymphocyte function, chemotaxis index (LCI), and proliferation (LP); and NK activity (lysis%).

The data was coded and entered into Statistical Package for Social Sciences (SPSS) version 23 for Statistical analysisAppropriate statistical tests were applied based on distribution and type of data. A p value of <0.05 was considered statistically significant.

Results

In this study, 50 patients who visited our antiaging unit in 2022 were included. The average age was 58 years old, with a 19% variation coefficient. Table 1 displays gender-specific data. There were no statistically significant age differences between men and women. Hormone levels were within normal limits for their ages (Table 1).

Table 1: Patient's data and hormonal values.

Patients	Men	Women	Reference values
Number	22	28	n.a.
Age	57.16 ± 10.13	59.31 ± 09.54	n.a.
Sexual hormones			
FSH (mUI/ml)	6.3 ± 4.7	89.9 ± 46.2	Men: 1.4–18.1 Women: 0.5–76*
LH (mUI/ml)	5.0 ± 9.2	40.43 ± 27.08	Men: 1.5–9.3 Women: 0.5–76*
Estradiol 17-β (pg/ml)	n.d.	111 ± 54.9	Women 11–196*
Progesterone (ng/ml)	n.d.	10.99 ± 6.3	Women: 1–20
Prolactin (ng/ml)	n.d	12.89 ± 6.0	Women: 1.8–29.2
Testosterone (ng/ml)	4.1 ± 2.17	n.d.	0.86–7.88
Thyroid hormones			
TSH (μUI/ml)	3.1 ± 7.4	3.0 ± 2.1	0.35–5.5
T4 (ng/dl)	1.2 ± 1.9	1.7 ± 0.7	0.78–1.8
Insulin (mg/dl)	79.5 ± 9.04	76 ± 10.98	60–100
IGF-I (ng/ml)	134.4 ± 66	121.2 ± 51.4	43–220

When we analyzed the levels of depression and stress in both men and women, we found that depression levels were significantly higher in women than in men ($p < 0.05$), mean difference 5.06; IC95% = -0.062–10.19 (**Table 2**).

Table 2: Stress levels:

	Men	Women	*p*
Stress -	0.38 ± 0.10	0.43 ± 0.16	0.473

We found that men showed significantly ($p < 0.05$) higher values in the NCI and LCI values than women (**Table 3)**. However, regarding PAN, LP, and NK activity, we did not find any significant differences.

Table 3: Immune status by sex.

Marker	Men	Women	*p*
NCI	476 ± 38.76	413 ± 20.00	**0.026**
PAN (a.u.)	259	176	0.845
LCI	277 ± 19.64	193 ± 11.74	**0.001**
LP (cpm)	19,673 ± 1,753	13,846 ± 1,650	0.382
NK (lysis %)	29 ± 7.97	54 ± 1.74	0.695

Then, we analyzed the possible correlation between stress and the different immunological markers under evaluation. We found a trend ($p = 0.048$) between NCI and this stress (**Table 4** and **Figure 3**). However, we did not find any correlation between PAN, LP, NK activity, and stress.

Table 4: Stress and immune marker correlations.

Marker	R Spearman	*p*
NCI	–0.251	0.048
PAN	–0.096	0.742
LCI	–0.054	0.093
LP (cpm)	–0.099	0.873
NK (lysis %)	–0.028	0.456

Discussion

Several studies have found that using social support techniques to improve one's psychological state is associated with an increase in survival in women with metastatic breast cancer or melanoma (Mustafa et al., 2013; National Collaborating Centre for Cancer [UK], 2015).[13-14] Furthermore, neuropsychological therapies involving physical exercise and various instruments for cognitive enhancement appear to decrease cognitive deterioration (Levin et al., 2017).[15] The usefulness of psychological therapies in changing a patient's biological status, on the other hand, is debatable. As a result, a recent meta-analysis of the association found minimal evidence linking the benefits of psychological treatments for depression to good biological outcomes. This lack of effect could be attributed to methodological flaws in the amended research (Cristea et al., 2019). [16]

The goal of this study was to characterise the state of immune response and its relationship to stress in a group of patients prior to their involvement in a psychological/physical programme meant to avoid physical and physiological deterioration. There were no statistically significant variations in age between men and women. In this study, we discovered significant gender disparities in NCI and LCI parameters, with men significantly higher than women. We must emphasise that our patients are stressed but not depressed or in the early stages of depression, and they are likely not immunologically damaged, making them suitable candidates for a preventative programme. Our premise was that we would uncover indicators of immune function decline in our patients. Indeed, we discovered a negative correlation between depression and NK activity, implying that a higher level of depression is associated with lower cytotoxic NK activity, which is consistent with previous reports (Zorrilla et al., 2001),[17] in which the authors reported in a meta-analysis review an overall leukocytosis, a reduced cytotoxic NK activity, and a higher level of depression. However, when we looked at whether there was a link between stress and NCI and gender, we only identified a significant link for women (Table 7). This could imply that women have a poorer neutrophil chemotaxis response, i.e., a lower response to infection. The negative link discovered between depression and NK activity, on the other hand, was shown to be irrespective of patient gender.

One study drawback is that our patients' ages are relatively homogenous (we have a variance coefficient of 19%), thus we cannot divide them into distinct groups based on this characteristic. In our group of individuals, however, we discovered a negative connection between age and NCI or PAN. This conclusion coincides with the commonly established fact that ageing deteriorates immune response (Fülöp et al., 2016).[18]

Another limitation of our study is that women outnumber men by about two to one. We recognise that this is not an ideal circumstance, and that the gender groups should be more homogeneous in order to draw more conclusive findings. Finally, we realise that the best strategy to analyse gender impact in our study is to use a regression model (moderation analysis) to determine whether gender is an independent component that causes changes in

stress, depression, and immunity. We were unable to conduct this analysis since the only demographic variable is "age," and we found no variations in this variable between men and women.

Conclusion

Our findings support previous findings that stress has an impact on the nonspecific immune system, namely the NK cytotoxic response. Another goal of this intervention would be to preserve and develop physical and cognitive capacities, allowing the patient's cancer therapy to go smoothly and so keep them better. In this regard, therapies such as a meditation exercise programme should be investigated as novel tools for reducing or preventing the impacts of stress. Careful monitoring of patient state will allow for a more accurate assessment of the outcomes of psychological programmes for stress and immune system status. As a result, we may be able to improve the life quality of patient.

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