The correlation of anxiety and depression levels with response to neoadjuvant chemotherapy in patients with breast cancer

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DECLARATIONS

Competing interests
None declared

Funding
None

Ethical approval
Ethical approval was not sought for this questionnaire study

Guarantor
CM

Contributorship
CM was the chief operating surgeon and conceived the study; RK and AG were involved in the data processing; MT, SJ, YK, NK, RB and SS collected the data and helped in the preparation of manuscript; SS was the pathologist in charge of the cases

Acknowledgements
None

Reviewer
Mohammed Rashed

Summary

Background The aim was to evaluate and correlate anxiety and depression levels with response to neoadjuvant chemotherapy in patients with breast cancer. The study also assessed the effects of family support on distress levels.

Design It was a prospective study in a cohort of 84 patients with locally advanced breast cancer. These assessments were done using the Hospital Anxiety and Depression Scale (HADS).

Setting A prospective study in a developing world setting.

Participants Eighty-four patients with locally advanced breast cancer receiving neoadjuvant chemotherapy were included after taking an informed consent and ethical committee clearance.

Main outcome measures A significant correlation was observed between response to neoadjuvant chemotherapy and depression levels in breast cancer patients. Joint family and literacy levels also had an impact on the levels of depression observed.

Results A total of 84 patients receiving neoadjuvant chemotherapy for breast cancer were evaluated using HADS. The effect of family support, literacy levels and employment on the psychological status of these patients were also assessed.

Conclusions The response to neoadjuvant chemotherapy had a direct correlation with the levels of depression, the distress levels being lower in responders. This was found to be the most important variable determining the psychological status of the patients. It was also observed that Indian patients in comparison to their Western counterparts react differently to cancer-related stress.

Background

Neoadjuvant chemotherapy is an integral part of the multi-modality approach to the management of locally advanced breast cancer.[1–5] Chemotherapy, which the patients are subjected to, involves long periods of treatment, repeated hospitalizations, and side-effects such as nausea, vomiting and alopecia. Cancer diagnosis and treatment have been shown to have profound effects on the psychological status of patients.[6–9] The initial response to a diagnosis of cancer ranges from shock and disbelief, to symptoms of dysphoria, irritability, loss of appetite and sleep disturbances. The intense chemotherapy administered can further add up to the psychological distress and the majority of these patients show adjustment disorders with symptoms of mixed anxiety and depression. Thus, the morbidity caused by cancer and its treatment is not entirely physical.[6–9] It has been observed that the psychological adjustment to cancer depends on several medical (stage of the disease, site and size of the tumor), sociocultural (attitudes, beliefs and means of support) and patient-related factors (personality types, coping mechanisms, pre-existing psychiatric illnesses).[6–8] There are numerous implications of distress and depressive states in cancer patients. These states, while acting as a burden for the patient and her family, also cause increased pain perception associated with longer hospital stays, decreased compliance to therapy and hence decreased response, and most importantly severe depression associated with an increased risk of suicide. Hence, it is essential to identify and appropriately manage the distress and depression in cancer patients in a timely manner.[6–8] In developed countries there are guidelines and protocols followed by a hierarchy of social workers and mental health professionals for the management of distress in cancer patients, for example the NCCN Guidelines in the USA and CAPO guidelines in Canada. But in developing countries where there are limited medical resources, distress management is mostly provided by the family members, traditional healers and religious workers.

With this background in mind, the present study was undertaken with the aim of assessing the levels of anxiety and depression in breast cancer patients in the Indian scenario and to correlate these levels with response to neoadjuvant chemotherapy. This was done by using the Hospital Anxiety and Depression Scale (HADS). We also tried to identify other contributing factors to the level of depression in these patients, such as education and employment of patients. To identify the effect of family support on the psychological status of patients, the correlation between depression and type of family (joint or nuclear) the patients belonged to, was also analysed.

Methodology

The levels of anxiety and depression of breast cancer patients in Safdarjung Hospital, New Delhi were assessed using the Hospital Anxiety and Depression Scale (HADS). HADS is a 14-item instrument designed to assess the levels of anxiety and depression. Each item was answered by the patient on a four-point (0–3) response category so the possible scores ranged from 0–21 for anxiety and 0–21 for depression. An analysis of scores on the two subscales of a further sample, in the same clinical setting, enabled provision of information that a score of 0–7 for either subscale could be regarded as being in the normal range, a score of 11 or higher indicating probable presence ('caseness') of the mood disorder and a score of 8–10 being just suggestive of the presence of the respective state.[9–11]

A total of 84 patients receiving neoadjuvant chemotherapy (CAF Regime) were evaluated. Written informed consent was taken and the patients were interviewed at each step of disease management, right from the time of diagnosis to get a baseline distress level, then after each cycle of neoadjuvant chemotherapy, post surgery, and after each cycle of chemotherapy. These interviews were carried out while the patients were waiting in day care for their session of chemotherapy. In addition to the HADS questionnaire, personal details like the demographic profile, religion, marital status and details of family were also collected after taking the informed consent from the patients.

The patients were categorized into two groups based on their response to therapy: responders and non-responders; the criteria for response

being a reduction of more than 50% in the tumor size on clinical assessment after three cycles of neoadjuvant chemotherapy. The levels of depression were correlated with the number of neoadjuvant chemotherapy cycles and the clinical response, education, occupation and the type of family the patient belonged to. Statistical analysis was carried out by using SPSS version 14.0.

Results

Cohort distribution

Based on the criterion stated above, 49 patients (58.3%) were found to be responders to the neoadjuvant chemotherapy, while 35 (41.7%) patients did not respond to chemotherapy. The majority of our patients were illiterate (46, 54.7%) and housewives (68, 79.7%). The distribution of patients into joint and nuclear families was equal (50% in each category).

As the patients were interviewed at each step of disease management, the number of neoadjuvant chemotherapy cycles received varied, and thus the effect of the number of cycles to response, toxicity and psychological status could be assessed. Fifty-one (60.7%) patients received three cycles or less of chemotherapy whereas 33 (39.3%) patients received more than three chemotherapy cycles. All 84 patients completed their scheduled neoadjuvant therapy.

Observations

None of the patients included in this study had any form of depression before the diagnosis of breast cancer. The mean depression scores in the breast cancer patients included in this study was 4.9 (range 1–6).

The mean depression score in responders after neoadjuvant chemotherapy was found to be 5.6 (range 1–16), whereas the mean score in non-responders was 10.2 (range 4–20).

Twenty-four (70.5%) non-responders were found to suffer from depression compared with only 11 (22.0%) of the responders (Table 1). Thus, the correlation of depression and response to neoadjuvant chemotherapy was found to be statistically significant (chi-square test, P value <0.05).

Seventeen (51.5%) of the 33 patients who received more than three neoadjuvant chemotherapy cycles showed depression, while 33 (64.7%) of the 51 patients who had received less than three cycles did not suffer from depression (Table 2). This correlation, however, was not found to be statistically significant. Thus, the number of cycles of neoadjuvant chemotherapy does not appear to be as important a criterion as the response to chemotherapy cycles for determining the psychological status of the patients.

Depression was found to be higher in literate (25, 54.3%) and employed (14, 53.8%) patients. However, these data were not found to be statistically significant.

An interesting observation in our study, was the effect of the type of family on the patient's psychological status (Table 3). It was seen that 24 (57.1%) patients from nuclear families showed significant levels of depression, in contrast to the 11 (36.2%) patients of joint families ($p < 0.05$). Thus, family support provided by the members appears to improve the psychological status of a cancer patient.

All patients completed their neoadjuvant chemotherapy regimes and there were no dropouts during this period on account of depression and/or anxiety.

Table 1
The presence or absence of depression in patients undergoing neoadjuvant chemotherapy

Depression	*Non-responder*	*Responder*	*Total*
No	10 (29.5%)	39 (78.0%)	49
Yes	24 (70.5%)	11 (22.0%)	35
Total	34	50	84

Table 2
The correlation between number of neoadjuvant chemotherapy cycles received and depression

Depression	*≤3*	*>3*	*Total*
No	33 (64.7%)	16 (48.5%)	49
Yes	18 (35.3%)	17 (51.5%)	35
Total	51	33	84

Table 3
The correlation between the type of family and depression in patients undergoing neoadjuvant chemotherapy

Depression	*Joint family*	*Nuclear family*	*Total*
No	31 (73.8%)	18 (42.9%)	49
Yes	11 (26.2%)	24 (57.1%)	35
Total	42	42	84

Discussion

The analysis of the data collected has shown that neoadjuvant chemotherapy had a physical as well as a psycho-social impact on patients. None of these patients had depression before the initiation of neoadjuvant chemotherapy, suggesting that neoadjuvant chemotherapy had a major role in the development of depression in some of the patients. Most patients were troubled by the side-effects of nausea and alopecia after the chemotherapy cycles, however, these lasted for a short duration, after which a significant proportion of patients were relieved and showed lower anxiety and depression levels due to the diminished lump size and reduced pain, an indication that they were likely to be cured of the deadly cancer. This observation was reflected in the finding that only 70.5% of non-responders were found to suffer from depression compared with only 22.0% of the responders. Thus, response to chemotherapy correlated significantly ($p < 0.05$) with the improvement in psychological status of our patients. Contrary to our expectations, none of the depressed patients were defaulters and this can be possibly explained, by the strong social support system available to them.

As compared to the results of the studies conducted in the developed world,[6–8] the Indian counterparts of breast cancer patients showed lower anxiety and depression levels. This can probably be attributed to their lower socioeconomic status (most patients in this study were in the lower middle and lower class according to the Kuppuswami scale), consequently leading to lower educational status. Being uneducated and not having much knowledge about the nature of the disease they were suffering from, lead to a carefree attitude about the illness. Another reason for the lower anxiety and depression levels in our patients could possibly be the presence of emotional and financial support offered by the family members of the patients, as it was observed in our study that a higher percentage of patients living in joint families showed lower rates of depression.

On the other hand, this lower literacy level also lead to few misconceptions about the disease, for instance, some patients thinking of cancer as a contagious disease which could spread by direct contact to their loved ones. This in turn leads to doubts and apprehensions, feelings of vulnerability and a tendency of social isolation.

Among other causes of anxiety and depression were worries concerning their households, loss of jobs leading to financial insecurity, and adjustment disorders on coming to a metropolitan city from a village. Many patients showed higher levels of anxiety for a few days before surgery.

Conclusions

Most Indian patients present as locally advanced breast cancer and require neoadjuvant chemotherapy, which improves the survival rates but has associated morbidity, which is not entirely physical. The response to neoadjuvant chemotherapy cycles has a direct correlation with depression, the distress levels being lower in responders. Statistically this was found to be the most important variable determining the psychological status of the patients. Although the distress levels were slightly higher in patients with more than three cycles on account of the increased side-effects of the drugs, this was not found to be statistically significant.

An association between socioeconomic status and levels of education, with anxiety and depression seems likely, however, a larger study group is required so that the significance of these preliminary results can be verified by statistical methods. Family support plays a vital role in improving the psychological status of the patients.

It seems that Indian patients in comparison to their Western counterparts react differently to cancer-related stress. Perhaps patients in the present study behaved differently than those in the West, thus 'a local solution to a local problem' is necessary requiring larger studies.

Many questionnaires devised in the West have been standardized to assess the psychological status of cancer patients throughout the world, one of which HADS was used in this study. But some questions seemed unsuitable for our patients; hence a questionnaire for the Indian set-up is desirable. A system for spreading awareness about breast cancer will go a long way in allaying the unfounded fears and misconceptions of our patients. Psychological interventions like psychotherapies, behavioral and relaxation techniques, art therapies and methods of spiritual healing can be tried to relieve the psychological distress, while patients with severe depression should seek psychiatric treatment including pharmacological agents.

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