Chapter I

Introduction
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**BACKGROUND OF THE STUDY**

**Prevalence of Breast Cancer**

American Cancer Society in its report states that malignant neoplasms are the second leading cause of mortality worldwide and breast cancer is most frequently diagnosed among women world over (estimated new cases in 2008 - 1,383,500). In developing countries, estimated new cases of breast cancer were 692,200 in the same year.\(^1\)

Even in Asian countries breast cancer incidence is increasing. The Singapore Malaysia Breast Cancer Working Group (SMBCWG), which is an international collaboration between the epidemiologists and oncologists of Singapore and Malaysia, merged the breast cancer registries of two academic hospitals in the two countries and analyzed data from 1990 to 2007. There were a total of 4058 patients from both the registries, registered between 1990 and 2007 from National University Health Systems or NUHS, Singapore (2545) and between 1993 and 2002 from University Malaya Medical Centre (1513). There were 8% women of Indian origin.\(^2\)

As mentioned by Badwe & Gupta in this editorial, the incidence of breast cancer has been increasing in India in the past few years and has overtaken uterine cervical cancer as the commonest cancer in women in metropolitan cities. The pattern of increase in breast cancer incidence is similar to that of United States that the maximum increase in incidence was seen among the postmenopausal women. But unlike in the US, India’s increasing incidence cannot be attributed to mass screening and over diagnosis.\(^3\)

Nandakumar reports in this article based on 2004–2005 data from population based cancer registries (PBCRs); that cancer breast has been ranked as a leading site of cancer in
most of the cities of India. The AAR (age adjusted rates) for breast cancer in Bangalore was reported as 27.5, Bhopal as 22.1, Chennai as 29.3, Delhi as 29.2 and Mumbai as 27.5. Reports from 2005–2006 data show an AAR of 19.6 in Aizawl district of Mizoram state with lower AARs in Kamrup Urban district (17.5) and Imphal west district (14.6).4


Breast cancer is conventionally treated with surgery, chemotherapy and radiation therapy. When the patient undergoes surgery, the type of mastectomy is decided by the stage of the disease, tumor grade, age and general health of the patient. Chemotherapy for breast cancer is administered to address the micro metastases and to prevent breast cancer recurrence and spread to other regions of the body. Breast cancer is treated with adjuvant radiation to prevent loco-regional recurrence of the tumor6.

Cancer Related Fatigue among Breast Cancer Patients

Almost all breast cancer patients experience fatigue during the course of treatment and the intensity of fatigue increases during the course of chemotherapy and radiotherapy. For most of us fatigue is relieved by a good night’s sleep. However, this is not the case for
patients undergoing cancer treatment. Fatigue is commonly seen as a debilitating side effect of cancer and its treatment and is frequently reported as a long term complication of various anticancer therapies. National Comprehensive Cancer Network has defined Cancer related fatigue as a “distressing persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning”.\textsuperscript{7}

Curt explains fatigue as a subjective and multi-dimensional concept with several modes of expression: physical, cognitive and affective. It can affect the patients’ sense of well-being, their ability to perform daily activities, the relationships with family and friends and even their ability to cope with the illness as well as to withstand the treatment.\textsuperscript{8} Hofman et al. identified cancer related fatigue as one of the most common and troublesome symptoms of cancer and side effect of cancer treatment along with pain and nausea.\textsuperscript{9}

Curt et al. in 2000 reported cancer related fatigue as very common in advanced cancers and its prevalence reported to be as high as 95\% among patients with advanced cancer receiving adjuvant therapies. They identified that cancer-related fatigue is a problem before, during and after therapy, and it can continue to be a problem in cancer survivors as well. Fatigue becomes pervasive, excessive, or constant and it interferes with participation in activities. Fatigue interferes with activities of daily living and patients reported an ability to accomplish 45\% of activities normally performed.\textsuperscript{10}

Lavdaniti in 2006 assessed fatigue and Health Status in Greek Patients with breast cancer undergoing adjuvant radiotherapy in a major oncology center, Saint Savvas Cancer Hospital, in Athens, Greece. Data were collected with the Revised Piper Fatigue Scale (PFS)
and the Short Form-36 (SF-36) Health Survey Scale in the first two days of radiotherapy, during the third week, and during the last week of treatment. It was observed that most of the patients experienced low levels of fatigue with a mean fatigue score of 1.96 (± 1.90). Only 13% of the women in the study experienced moderate to high levels of fatigue. It was also shown that fatigue increased during radiotherapy in patients with breast cancer regardless of stage, type of surgery, or whether they received chemotherapy.\textsuperscript{11}

Cancer-related fatigue has a very strong negative effect on quality of life as the ability of cancer patients to engage in normal activities and carry out their activities of daily living and usual role function decline as the treatment progresses. Thus cancer related fatigue a problem often less understood and underdiagnosed, should be considered as an important issue to challenge during cancer and its treatment.\textsuperscript{8}

As discussed by Victoria Mock in 2003, the exact mechanisms involved in the development of cancer-related fatigue are not completely known; but the physiological factors that contribute to the development of fatigue are inter-related, complex and include anaemia, cancer therapy, cachexia, tumour burden, and the release of cytokines. As the exact pathophysiological mechanisms are unknown, there is no specific evidenced-based intervention to prevent the development of cancer-related fatigue. The approach to the management of cancer related fatigue is a general one and different interventions like education, exercise, rest and sleep, energy conservation, stress reduction etc were tried out to treat cancer related fatigue.\textsuperscript{12}
Yoga and Pranayama as an intervention for Cancer Related Fatigue

Carson in their pilot study examined a yoga-based palliative intervention, the Yoga of Awareness Program, in a sample of women with Metastatic Breast Cancer (MBC) in 2007. Twenty one adult women with MBC referred by oncologists at the Duke University Medical Center breast oncology unit and affiliate sites performed gentle yoga postures, breathing exercises, meditation, didactic presentations, and group interchange for eight weeks. Outcome was assessed using daily measures of pain, fatigue, distress, invigoration, acceptance, and relaxation during two pre-intervention weeks and the final two weeks of the intervention. Lagged analyses of length of home yoga practice showed that on the day after a day during which women practiced more, they experienced significantly lower levels of pain and fatigue, and higher levels of invigoration, acceptance, and relaxation.13

Bower et al. conducted a randomised controlled trial at the University of California-Los Angeles (UCLA) among breast cancer survivors with persistent post-treatment fatigue in 2012. In this study, experimental group of patients received Iyengar yoga classes for 12 weeks whereas the control group received health education for 120 minutes once in a week for 12 weeks. Outcome measures were obtained at baseline, within 2 weeks post intervention, and 3 months after the intervention was completed. It was found that Yoga resulted in statistically significant improvements in fatigue severity and vigor.14

Antioxidant effect of Yoga and Pranayama

Apart from reducing the cancer related fatigue and improving the vigour of patients suffering from cancer, Pranayama can influence the antioxidant status of human body. An antioxidant is a substance that scavenges free radicals. The body endogenously produce non-
enzymatic antioxidants such as glutathione (GSH) and enzymatic antioxidants such as superoxide dismutase (SOD), catalase, glutathione reductase and glutathione peroxidase. Balance between the levels of free radicals and antioxidant defence is very essential for a healthy human body. Sinha et al have found that there was an improvement in the level of glutathione and total antioxidant status with yoga and Pranayama among healthy people. In this study, fifty one healthy male volunteers from the Indian Navy, Delhi were divided into two groups-a yoga group (n = 30) and a control group (n = 21) by the researchers in 2007. The yoga group performed Yogasanas and Pranayama for one hour in the morning, five days per week for six months whereas the control group practised routine physical exercises. After completion of six months of training, fasting blood samples were analysed for reduced glutathione (GSH), oxidized glutathione (GSSG), glutathione reductase (GR), activity, and total antioxidant activity (TAS). It was found that level of glutathione increased significantly from the baseline value of 235.3-16.9 nmol/L to 331.7 - 37.6 nmol/L in the yoga group.

Pranayama has antioxidant effect not only on healthy people but also on patients suffering from serious illnesses. It was found to raise anti-oxidant enzymes in a sample of patients suffering from coronary artery disease. Nikam et al assessed the effect of Pranayama practicing on lipid peroxidation and antioxidants in coronary artery disease (CAD) in 2010 at the outpatient department of District Hospital, Belgaum, Karnataka, India. Out of the 60 patients, 30 patients were practicing Bhashrika Pranayama, Kapalbhati Pranayama, Bhya Pranayama, Anulom-vilom Pranayama and Brahmari Pranayama and the other 30 were kept on drug therapy. The fasting venous blood samples obtained from these subjects were analysed for the activity of enzymatic antioxidants superoxide dismutase [SOD], glutathione peroxidase [GPx] and catalase before starting the practise and at the end
of 4, 6 and 8 weeks of practicing pranayama. In CAD patients there was significantly decreased activity of catalase and GPx and Superoxide dismutase in the beginning. This lowered activity of SOD, GPx and catalase were significantly raised after practicing 4 and 6 weeks of these five pranayama and it became within normal range after 8 weeks.\textsuperscript{16}

It was observed by the researcher that a considerable number of cancer patients being treated in the present setting also suffer from fatigue. But there are not many published studies done in India especially in Karnataka assessing the prevalence of cancer related fatigue or exploring the mechanisms behind the development of cancer related fatigue. Encouraged by the results shown by studies employing pranayama to relieve fatigue and to improve the antioxidant status among varied populations, the researcher attempted to test the effectiveness of pranayama on cancer related fatigue and antioxidant status among breast cancer patients undergoing radiation therapy

**Statement of the problem**

Effectiveness of Pranayama on cancer related fatigue and selected biochemical parameters among patients with breast cancer undergoing radiation therapy in Shirdi Sai Baba Cancer Hospital & Research Centre, Kasturba hospital, Manipal

**Purpose of the Study**

Cancer patients while undergoing treatment suffer from a number of side effects. Patients all over the world look for ways to reduce the side effects of cancer treatment. Many opt for various complementary and alternative therapies. The present study attempted to determine the effectiveness of Pranayama (a complementary therapy) on side effects of radiation therapy like cancer related fatigue among breast cancer patients. The study further
explored the level of selected non-enzymatic antioxidants and antioxidant enzymes among these patients with or without performing Pranayama in an effort to identify the possible mechanisms behind the development of cancer related fatigue. It also explored the relationship between the level of glutathione (GSH), an antioxidant and cancer related fatigue.

The long term focus is to know whether these kinds of complementary therapies can be employed to relieve or reduce the side effects of cancer treatment without interfering with the desirable effects of treatment. If found effective, Pranayama can be utilized by breast cancer patients undergoing radiation therapy as a supportive measure.

**Objectives of the Study**

**The objectives of the study were to:**

1. determine the effectiveness of Pranayama on
   1.1 cancer related fatigue among breast cancer patients undergoing radiation therapy as measured by cancer fatigue scale.
   1.2 selected biochemical parameters among breast cancer patients undergoing radiation therapy.

2. determine the relationship between cancer related fatigue and the level of glutathione (GSH) and its associated enzymes among breast cancer patients undergoing radiation therapy.

**Assumptions**

1. Breast cancer patients undergoing radiation therapy experience some amount of fatigue.
2. Lack of antioxidants and antioxidant enzymes increase the side effects related to cancer treatments.

3. Antioxidants and antioxidant enzymes could be playing a role in the development of cancer related fatigue among breast cancer patients undergoing radiation therapy.

4. There is possibly a relationship between the level of glutathione (GSH) in the body and cancer related fatigue among breast cancer patients undergoing radiation therapy.

5. Pranayama may reduce the amount of cancer related fatigue experienced by breast cancer patients undergoing radiation therapy.

6. Pranayama may influence the level of antioxidants and antioxidant enzymes in the body of breast cancer patients.

**Hypotheses**

**The hypotheses will be tested at 0.05 level of significance**

**H$_1$**: There will be a significant difference in the pretest and post-test scores of cancer related fatigue among the experimental group as measured by cancer fatigue scale.

**H$_{1.1}$**: There will be significant difference in the scores of cancer related fatigue between the experimental group and control group as measured by cancer fatigue scale at the completion of radiation therapy.

**H$_2$**: There will be a significant difference in the pretest and post-test level of serum protein thiols among the experimental group.

**H$_{2.1}$**: There will be significant difference in the level of serum protein thiols between the experimental group and control group at the completion of radiation therapy.

**H$_3$**: There will be a significant difference in the pretest and post-test level of glutathione (GSH) among the experimental group.
H₃.1: There will be significant difference in the level of glutathione (GSH) between the experimental group and control group at the completion of radiation therapy.

H₄: There will be a significant difference in the pretest and post-test level of serum glutathione S transferase among the experimental group.

H₄.₁: There will be significant difference in the level of serum glutathione S transferase between the experimental group and control group at the completion of radiation therapy.

H₅: There will be a significant difference in the pretest and post-test level of glutathione reductase among the experimental group.

H₅.₁: There will be significant difference in the level of glutathione reductase between the experimental group and control group at the completion of radiation therapy.

H₆: There will be a significant difference in the pretest and post-test level of glutathione peroxidase among the experimental group.

H₆.₁: There will be significant difference in the level of glutathione peroxidase between the experimental group and control group at the completion of radiation therapy.

H₇: There will be a significant relationship between the scores of cancer related fatigue and the level of glutathione (GSH).

H₇.₁: There will be a significant relationship between the scores of cancer related fatigue and the level of protein thiols.

H₇.₂: There will be a significant relationship between the scores of cancer related fatigue and the level of glutathione S transferase.

H₇.₃: There will be a significant relationship between the scores of cancer related fatigue and the level of glutathione peroxidase.
H7.4: There will be a significant relationship between the scores of cancer related fatigue and the level of glutathione reductase

**Operational Definitions**

**Pranayama:** BKS Iyengar in his book “Light on Pranayama” defines Pranayama. ‘Prana’ means breath, respiration, life, vitality, energy or strength. When used in the pleural, it denotes certain vital breaths or currents of energy (prana - vayus). ‘ayama’ means stretch, extension, expansion, length, breadth, regulation, prolongation, restraint or control. ‘Pranayama’ thus means the prolongation of breath and its restraint.\(^{17}\)

**Pranayama:** In this study, Pranayama refers to the yogic breathing exercises like Brahmari, Sheethali and Nadi sodhana Pranayama. In Brahmari Pranayama, the technique is to concentrate on the inhalations and exhalations with a humming sound. In Sheethali Pranayama, deep inhalations are taken through curled tongue which is stretched out of mouth and in Nadi shodhana Pranayama deep and steady inhalations and exhalations are taken through alternate nostrils. The exact procedures of these three techniques are given in appendix.

**Biochemical parameters:** included antioxidant enzymes like glutathione reductase, glutathione peroxidase, glutathione S transferase, and non-enzymatic antioxidants like protein thiols and glutathione (GSH).

**Cancer related fatigue:** National Comprehensive Cancer Network\(^7\) defined cancer related fatigue as a “distressing persistent, subjective sense of physical, emotional and / or cognitive tiredness or exhaustion related to cancer or cancer treatments that is not proportional to recent activity and interferes with usual functioning”.

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In this study Cancer related fatigue refers to the fatigue experienced and reported by breast cancer patients undergoing radiation therapy and as measured by cancer fatigue scale. 

**Radiation therapy:** In this study radiation therapy refers to post-operative adjuvant radiation therapy for breast cancer patients.

**Conceptual Framework**

The present study has adapted Lydia E Hall’s\(^1\) theory of Care, Core and Cure and competition model of radio protection by Urtasun RC and Brown JM\(^2\). Lydia Hall has used three interlocking circles to present her theory. Each circle represented aspects of nursing like care, core and cure. CARE is the sole function of nurses, whereas the CORE and CURE are shared with other members of the health team. Competition model is incorporated in the cure circle. The competition model proposes that endogenous sulphydryl scavenge free radicals and repair the damaged DNA in radiation. In radiation, protection of normal tissues to the exclusion of tumor tissues is essential to improve the therapeutic ratio.

**The core circle**

In the core circle the nurse helps the patient to identify his/ her own self, helps to explore and express their feelings regarding current health status and the potential changes in lifestyle. Here the patient becomes aware of the feelings and changes experienced and become capable of taking conscious decisions. This will further help the patient to recognize the motivation and energy necessary for healing which exists within him.

In the present study, the core circle represents the breast cancer patient undergoing radiation therapy. This also denotes the physical, functional, affective and the cognitive
aspects of the patient which contribute to fatigue. Here, while assessing the cancer related fatigue, the patient was helped to explore and express her subjective experiences regarding the various abovementioned aspects of cancer related fatigue.

**The Care Circle**

It is the nurturing component of nursing and is exclusive to nursing. Nurturing involves the direct bodily patient care, to assist in the basic biological functions and to provide for teaching learning activities. Providing bodily care makes the patient closer to the nurses and the patient shares the feelings with the nurse. While providing this care the nurse maintains a professional status rather than a mothering status and uses her strong theoretical knowledge base to guide the patient and to care for him.

Pranayama is the care offered to the breast cancer patients of the present study. Pranayama improved the breast cancer patient’s fatigue level. Since these patients were coming together at one place to practice Pranayama, they shared a feeling of togetherness and shared and discussed their problems.

**The Cure Circle**

The cure, on the other hand is the attention given to the patients by the nurse based on her knowledge of disease conditions and pathophysiology and it is shared with other medical professionals. The nurse helps the patient and family through the procedures required for curing the disease and the prescriptions made by the physician.

The cure circle in this study is explained by incorporating the competition model of radio protection by Urtasun and Brown. Competition model states that glutathione is the major endogenous sulfhydryl. Intracellular sulfhydryl scavenge free radicals and repair the damaged DNA in radiation. In radiation, protection of normal tissues to the exclusion of
tumor tissues is essential to improve the therapeutic ratio. The assumption that tumor tissues are not protected to the same degree as normal tissues by endogenous sulfhydryl is based on the fact that tumors have hypoxic regions and poor blood perfusion.

In this study, the breast cancer patients who were selected were after surgical treatment for breast cancer and adjuvant chemotherapy. Patients were recruited when they were admitted for radiation therapy. Radiation therapy uses photon energy to cause DNA damage to cancer cells. During this process, normal tissues are also damaged by photon energy. Endogenous sulfhydryls like glutathione (GSH) protect the cells against DNA damage by scavenging the free radicals and repairing DNA damage. Pranayama increases the level of glutathione in the blood of breast cancer patients. Even though cancer treatments aim for curing the disease in the patients, they cause some unwanted effects in the patients. Pranayama as a complementary treatment increases the level of endogenous sulfhydryls like glutathione.
Fig 1: Conceptual Framework based on Lydia E Hall’s theory of Care, Core and Cure and competition model of radio protection by Urtasun and Brown
Variables

**Dependent variables:** Cancer related fatigue, selected biochemical parameters.

**Independent variable:** Pranayama

**Delimitation**

The study is delimited to breast cancer patients undergoing radiation therapy in Shirdi Sai Baba Cancer Hospital & Research Centre, Kasturba hospital, Manipal

**Summary**

This chapter dealt with background of the study, statement of the problem, purpose of the study, objectives, assumptions, hypothesis, variables, operational definitions, conceptual framework and delimitation of the study.

**Outline of the Study**

The report of the study is presented in the following chapters:

- **Chapter II: Review of literature** - Presents an overview of the related literature - original scientific research articles and non-research literature.

- **Chapter III: Methodology**: deals with data collection process and plan for data analysis

- **Chapter IV: Analysis and Interpretation**: This chapter presents data analysis, interpretation of data and discussion

- **Chapter V: Summary, Findings and Conclusion**: Presents major findings of the analysis of data, conclusion and implications to nursing education, research and administration. Limitations of the present study and recommendations derived for further study are included in this chapter.