

CHAPTER III

MATERIAL AND METHODS

The present study was done in the cancer Research Institute, SRHU, Swami Ram Nagar, Dehradun over a period of two years (January 2013 to March 2015). The female patients diagnosed with cancer of breast, had undergone breast surgery and came for receiving their first cycle of chemotherapy were recruited in the study.

Research Approach: The quantitative research approach was adopted in this study

Research Design: The Randomized Clinical Controlled Trial with Time series design was adopted in the present study.

Randomization	Control Group	Cycle I O1	Cycle II O2	Cycle III O3	Cycle IV O4	Cycle V O5	Cycle VI O6
	Experimental Group	Cycle I O1 X1	Cycle II O2 X2	Cycle III O3 X3	Cycle IV O4 X4	Cycle V O5 X5	Cycle VI O6 X6
	Time of assessment	Baseline Assessment	After 21days of cycle I	After 21days of cycle II	After 21days of cycle III	After 21days of cycle IV	After 21days of cycle V

Where

Cycle I-VI=Chemotherapy cycles

O1-O6= Assessment of stress level and Quality of life of breast cancer patients in control and experiment groups

X1-X6=Yoga Intervention given to experimental group

Time of assessment: Assessment of stress level and Quality of life was done at cycle one and then after 21 days

Variables: In the present study there were the following variables-

1. **Sociodemographic variables-** Described the characteristics of breast cancer patients undergoing chemotherapy including age, educational status, occupation,

source of income, marital status, number of children, living status, co-morbidity, history of substance use, family history, heard about cancer of breast.

2. **Clinical variables-** Described the clinical status of breast cancer patients undergoing chemotherapy, including menopausal state, grade of cancer, type of breast surgery and type of chemotherapy regimen received.

3. **Independent Variable-** In the present study the Independent variable was

Yoga- The term yoga has come from the Sanskrit root “Yuj” means union. Yoga is systematic application of certain practices which are researched and found to be having effects and benefits in human body. (Rama S. 1992) . Yoga involves far more than just physical asanas. It is deeply imbedded in mind and body correlation. The yoga intervention consisted of diaphragmatic breathing, systematic relaxation, alternate nostril breathing, Joints and glands exercises of neck and shoulder. These exercises were extrapolated from three sources. The references are listed in booklet. For clear picture illustration please refer to booklet which describes the whole intervention.

Diaphragmatic breathing- According to the literature diaphragmatic breathing is considered to be the essence of relaxation. It promotes a natural and smooth breath movement that strengthens the autonomic nervous system and relaxes the body. In diaphragmatic breathing the lungs fill completely, providing the body with sufficient oxygen and forces the carbon dioxide out from the lungs. When we breathe diaphragmatically, the lower ribs flairs out slightly on inhalation, and the abdominal area also moves out a bit. On exhalation, the abdominal area moves back in towards the spinal column (Rama S.1992).

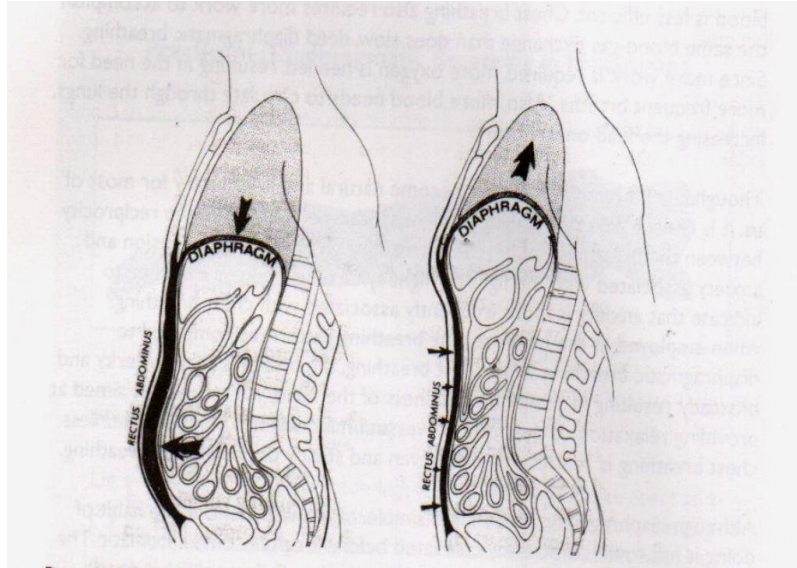


Figure 2: Movement of the diaphragm and the abdominal wall during inhalation and exhalation (Keshaviah P (2016))

Systematic relaxation- It is one form of relaxation technique which relaxes the skeletal muscles, eliminates any fatigue or strain and enhances the parasympathetic component of the autonomous nervous system. (Rama S.1992).

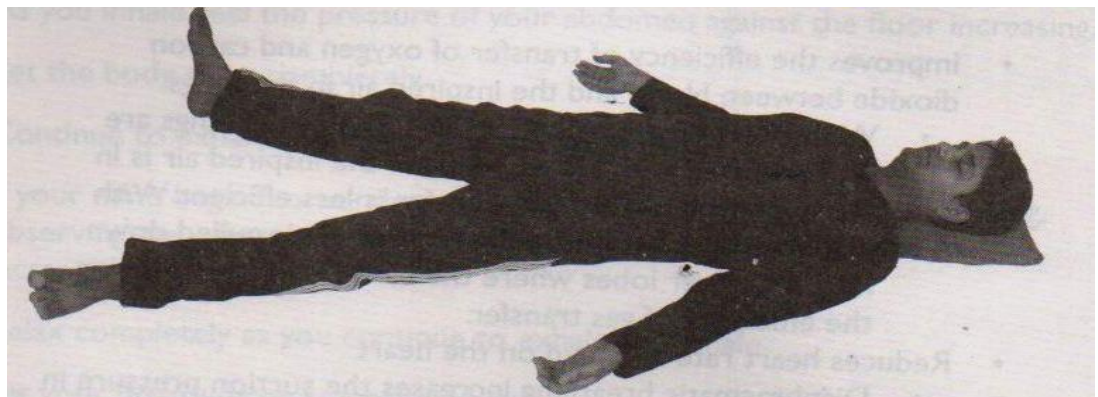


Figure 3: Systematic Relaxation in Shavasana position (Keshaviah P (2016))

Alternate Nostril Breathing- It is a simple pranayama exercise that purifies the nadi, the subtle energy channels. It balances the flow of breath in the nostrils and the flow of energy in the energy channel. Nadi shodhanam, a technique in which one deliberately changes the flow of air

from one side to the other, regularly and rhythmically, through exerting pressure on the valve or lateral wall of one nostril or the other. It is said to purify and balance the nadis, the subtle energy channels. It balances the flow of breath in the nostrils and the flow of energy in the energy channel. It creates a state of clarity and serenity. It also seems to help balance the functioning of the autonomic nervous system. (Rama S.1992)

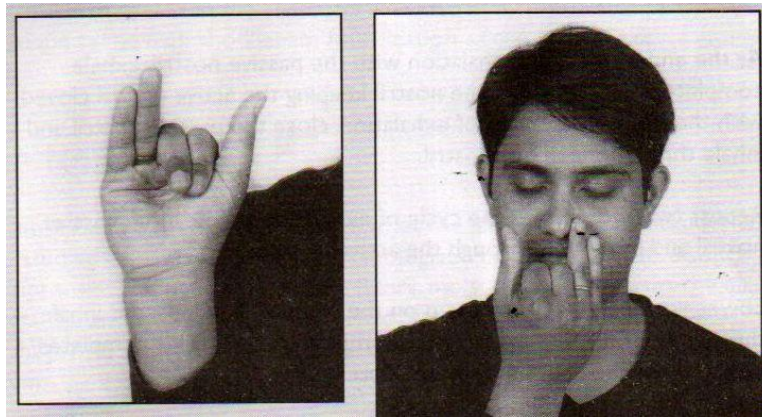


Figure 4: Alternate nostril breathing (Keshaviah P (2016))

Joints and Glands Exercises for the Neck and Shoulder- The joints and glands exercises, resembles the upper body range of motion exercises. The main purpose of joints and glands exercises is that it affects the lymphatic system which positively affects the immune system. They are not asanas. For more complete description please refer to the appendix.

4. **Dependent variable** – In the present study dependent variables were-

- (i) **Stress level:** Stress is defined as the activation of the arousal mechanism, especially the alarm mechanism defined as fight or flight. This physiological response to the perception of threat is mediated by the sensory-motor system and the sympathetic part of the autonomic nervous system in particular. (Nuernbergers P. 1981).
- (ii) **Quality of life-** According to WHO quality of life is a person's understanding of his placement in life which refers to the culture, belief systems in which he exists and with regards to his aim, anticipation, social level and interest.

(WHO QOL 1993). In the present study the quality of life means physical, psychological and social aspects of health.

Setting of the study: The present study was done at the Cancer Research Institute, a unit of Himalayan Hospital. The institute addresses to early detection, treatment and research in cancer. It has been providing diagnostic services as well as treatment facilities for all types of cancer such as surgery, chemotherapy and radiation therapy through its specialty departments such as nuclear medicine, Oncosurgery, day care and in patient chemotherapy, and radiotherapy. The weekly census for day care unit for chemotherapy is around 80-85 patients and 400 patients per month. The number of breast cancer patients coming to day care for chemotherapy is around 20 patients per week and 70 patients per month. The census of in-patients in cancer research institute is around 350 patients per day and more than 1000 patients per month. It is also a nodal center for referral of cancer patients in the states of Uttarakhand, Uttar Pradesh, and Haryana etc.

Population: The population of the present study comprised of female patients diagnosed with breast cancer and undergoing treatment in Cancer Research Institute, Swami Rama Himalayan University.

Sample: The sample of the present study were female patients diagnosed with breast cancer and undergoing chemotherapy in Cancer Research Institute, Swami Rama Himalayan University, were selected as sample in the study.

Sample size Calculation: Sample size was calculated on the basis of previously published literature (Vadiraja SH et al. (2009), considering psychological distress, physical distress and insomnia parameters to estimate sample size as primary outcome. Mean± SD from the above mentioned literature was used to achieve 80 % power (β) at 5% level of significance (α). Considering 10 % dropout the researcher enrolled 50 patients in both experimental and control group. Formula for sample size calculation used was as follows.

$$N = \left[\left(\frac{Z_{\alpha} + Z_{\beta}}{\delta} \right) \sigma \right]^2$$

Sample size: Total 100 breast cancer patients, who were receiving six cycles of chemotherapy were recruited in the present study.

Sampling Technique- Consecutive sampling technique was adopted in the study to recruit the sample. In that all the breast cancer patients who were coming to Day Care Center for chemotherapy and were fulfilling the inclusion criteria were included in the study. The eligible sample was randomized into control and experimental groups by concealed randomization, by using sealed numbered envelopes. The investigator prepared these envelopes with the help of a colleague. As the study participants were available the investigator opened the sealed numbered envelope in which group name was written and assigned the patient to that group.

Sampling criteria: Following inclusion and exclusion criteria were used to take the sample in the study.

Inclusion Criteria: The following criteria were kept under consideration for selecting the sample. Females breast cancer patients of all age groups who:

1. Had undergone breast surgery as primary treatment and were scheduled for receiving adjuvant chemotherapy.
2. Were agreed to take part in the study.
3. Were not practicing yoga.
4. Could follow instructions related to yoga in Hindi language.
5. Were willing to practice yoga regularly at home.
6. Had Zubrod's performance status score 0-2. This means that they were able to walk about more than fifty percent of the time.

Exclusion Criteria: Breast cancer patients were not included in the study if they -

1. Had any known metastasis.
2. Received chemotherapy before surgery and after radiotherapy.

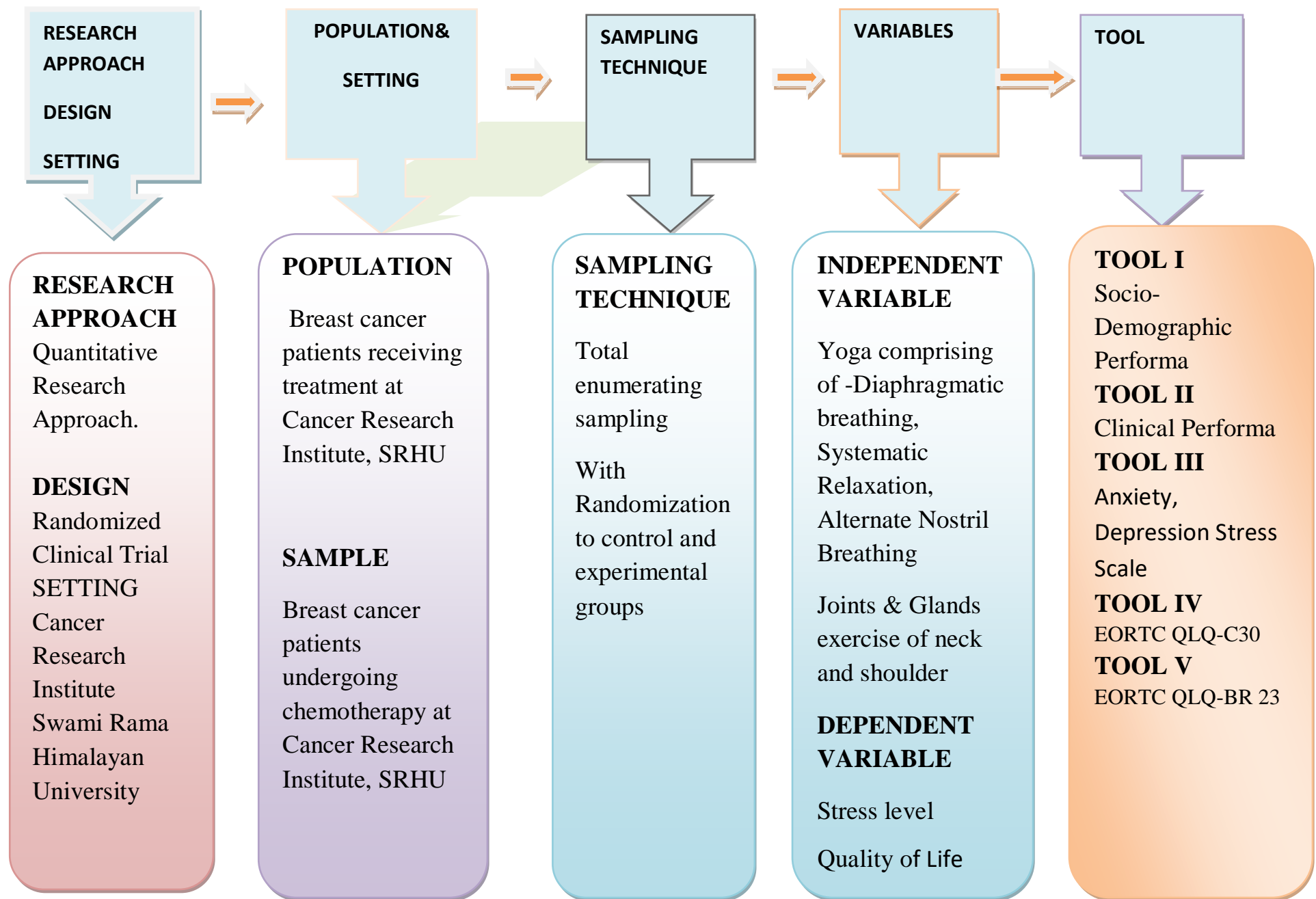


FIGURE 5:- SCHEMATIC REPRESENTATION OF RESEARCH DESIGN

Description of the Tools: In the present study the following tools were used to collect data

1. Socio demographic and clinical Proforma
2. Eastern Cooperative Oncology Group (ECOG, Zubrod) performance scale
3. Hindi version of ADSS (Anxiety Depression and stress Scale)
4. Hindi Version of European Organization for Research and Treatment of Cancer Quality of Life Tool- EORTC QLQ-C30 (version 3)
5. Hindi Version of EORTC QLQ - BR23 (Breast cancer module)
6. Record sheet of yoga practice

Description of tool 1: Socio-demographic and clinical Proforma

The Socio-demographic variables included were- age, educational status, occupation, source of income, marital status, number of children, living status, co-morbidity, history of substance use, history of cancer in the family, practicing yoga presently, heard about breast cancer.

The clinical variables included were-menopausal status, grade of cancer, type of breast surgery and type of chemotherapy regimen received.

Description of tool 2- Eastern Cooperative Oncology Group (ECOG, Zubrod) performance scale (Oken MM, et al. 1982). This tool assesses performance status of patients and range from fully active scored zero to completely disabled scored four.

Description of tool 3- ADSS-BSPSA (By Pallavi Bhatnagar, et al. Anxiety, Depression and Stress Scale).

ADSS consisted of a total of 48 items, which were separated in three subscales:

1. Anxiety subscale – it consisted of 19 items, which measured a variety of symptoms that are expressions of anxiety.
2. Depression subscale – it consisted of 15 items exhibiting the different symptoms of depression.
3. Stress subscale – it consisted of 14 items which covered the symptoms that an individual has when he is in stress.

Reliability of Anxiety, Depression and Stress Scale

Reliability of the entire scale as expressed by internal consistency calculated by Cronbach's Alpha and Spearman-Brown coefficient was 0.81 and 0.89. The reliability for anxiety, depression and stress subscales calculated by Cronbach's Alpha was 0.76, 0.75 and 0.61 respectively and as calculated by Spearman-Brown coefficient was 0.86, 0.86, and 0.76 respectively

Scoring & Interpretation of (ADSS)—Reply of the items were in terms of 'Yes' or 'No'. Each item was scored 01 (one) if endorsed "Yes" and 0 if endorsed "No". The range of the score was 0-19 for anxiety subscale, 0-15 for depression subscale and 0-14 for stress subscale. Higher score indicated experiencing greater anxiety, higher depression and higher stress and lower score indicated less anxiety, less depression and less stress.

Investigator had purchased the tool ADSS to use in the study for data collection.

Description of tool 4- European Organization for Research and Treatment of Cancer Quality of Life Tool- EORTC QLQ-C30 (version 3)

The QLQ – C30 is a questionnaire for evaluating quality of life in cancer patients. It consisted of total 30 items.

- ❖ Global health status scale=2 items
- ❖ Five functional scales (physical, role, emotional, cognitive and social)= 15 items
- ❖ symptoms scales associated with cancer and treatment (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea and financial difficulty)=13 items

For the functional and symptoms scales the response design was a 4-point Likert type (from "not at all" to "very much") and for global health status it was 7 point linear analogue scale (from "bad" to "optimum").

Description of tool 5- European Organization for Research and Treatment of Cancer Breast cancer module: QLQ-BR23

It consisted of total 23 items.

- ❖ Four functional scales (body image, sexual functioning, sexual enjoyment, future perspective)= 8 items
- ❖ symptoms scales (systemic therapy side effect, breast symptom, arm symptom, upset by hair loss)=15 items

The functional and symptoms scales response layout was a 4-point Likert type (from “not at all” to “very much”)

Reliability and Validity QLQ C-30 & BR-23

Parmar V et al. (2005) validated EORTC quality-of-life questionnaire. The reliability and validity of English and Hindi translated version was tested using Cronbach alpha (0.61-0.96) and item-scale correlation (0.63-0.93) and concluded that QLQ- C 30 and BR- 23 questionnaire could be used to assess quality of life in cancer patients of our country India.

Scoring & Interpretation– The EORTC QLQ-C30 and EORTC QLQ-BR23 items were scored according to EORTC Scoring Manual. Later scores were linearly converted to range between 0–100. Higher score represented a higher ("better") stage of ability to function and Global Health Status. A high symptom score represented that symptoms were at the “worse” level.

Description of tool 6: A record sheet of yoga practice was given to the patients in the experimental group to record practice of yoga done by them at home daily in the morning and evening.

Development of Intervention on yoga

The intervention on yoga was developed by referring to related literature, research studies, and discussion with experts.

The yoga intervention protocol consisted of four components. (Please refer to Annexure for detail description)

1. Diaphragmatic Breathing
2. Systematic Relaxation
3. Alternate Nostril Breathing
4. Joints and glands exercises for the neck and shoulder

The investigator attended classes to learn and practice yoga conducted by a certified yoga teacher at Swami Rama Himalayan University. Under her guidance and help, the investigator prepared a booklet for patients on “Yoga during chemotherapy”. The booklet contained information on diaphragmatic breathing, systematic relaxation, alternate nostril breathing & joints and glands exercises for the neck and shoulder with reference from

books written by Swami Rama on “Science of Breath”, “meditation and Practice” and “Joints and Glands”. The above listed books came from the Himalayan tradition and this treatment protocol was designed and taught by a certified teacher from the same Himalayan yoga tradition of the author of the above books. The investigator taught yoga to breast cancer patients in the experimental group under the supervision of above mentioned yoga teacher.

Content validity of the booklet on “yoga during chemotherapy” was established by giving it to experts from the field of Yoga and Nursing. Their suggestions were integrated in the booklet.

Validity of the tools:

Content validity of the tools and booklet on “yoga during chemotherapy” was established by giving them to experts from the field of Yoga and Nursing. Their suggestions were integrated in the tools and booklet. Tool to assess stress level and quality of life were standardized tools.

Pretesting of the tool

The socio-demographic and clinical questionnaire and Hindi version of quality of Life tools-QLQ C30, BR 23 & ADSS (Anxiety Depression Stress scales) were given to 10 breast cancer patients undergoing chemotherapy to fill. They did not have any difficulty in understanding the question. Participants took 15 minutes to fill the tools.

Pilot Study

Pilot study was carried out in the month of November-December 2012. Permission was obtained from Ethical Committee of University and Director, CRI. Ten patients who were receiving chemotherapy for breast cancer were included in the study, five in experimental and control group each. Yoga was taught to patients who were in experimental group and patients in control group routine care. Patients in both groups were followed for two cycles of chemotherapy. Stress level and quality of life was assessed two times. The study was found to be feasible.

The problem faced by investigator during pilot study- The study required more time as time series design was used.

Ethical consideration

1. Ethical permission was obtained from Ethical committee of Swami Rama Himalayan University.
2. Written informed consent was taken from each sample.
3. Anonymity of study subjects was maintained.
4. Data gathered were kept confidential.
5. Participants were allowed to discontinue the study at whichever time they wished.
6. They were assured of no harm.

Administrative permission

Administrative permission was taken from:

1. Chairperson PhD committee & Registrar, Swami Rama Himalayan University.
2. Director, Cancer Research Institute.

Data Collection Procedure/Study Protocol

Sealed envelopes with numbers written on them were prepared for concealed randomization of study participants to control and experimental groups.

All participants who participated in the study were able to move around their own. Their Zubrod's performance status score was between 0—2.

The investigator identified the eligible participants based on the inclusion and exclusion criteria and randomized them into control and experimental groups. The researcher explained the reasons for conducting study and process of the data collection to the patients and their accompanying relatives. Thereafter the investigator explained the consent form to the patients and their relatives. Assurance was given to them that their information would be kept confidential and they could leave the study whenever they wished. They signed consent form to show their willingness to partake in the study.

During the first chemotherapy cycle, the investigator met the participants and handed out the socio-demographic and clinical proforma, QLQ C 30, BR23 and ADSS questionnaire to study participants in the experimental and the control group. All patients who could read and understand the Hindi language filled the questionnaire by themselves. The investigator assisted those study participants, who could not read Hindi,

in filling the questionnaire by reading the questionnaire to them and asking them to tick the option best suited them.

Following that, the investigator explained the benefits of performing yoga during the period of receiving chemotherapy to patients in the experimental group and taught them yoga by demonstrating the steps of diaphragmatic breathing, systematic relaxation, alternate nostril breathing, & neck and shoulder exercises. The return demonstration was done by participants in front of the investigator. The researcher spent two hours with study participants who were in the experimental group during the first cycle of chemotherapy.

The researcher provided each one of them a booklet on “Yoga during chemotherapy” which contained information regarding steps of performing diaphragmatic breathing, systematic relaxation, alternate nostril breathing & joints and glands exercises of neck and shoulder, in words and pictorial form. Participants were asked to practice the above mentioned steps twice daily (morning & evening) at home and to maintain a record of the same.

The investigator met participants of both groups when they came after 21 days for their next second, third, fourth, fifth and sixth cycles of chemotherapy and gave them Hindi versions of QLQC 30, BR-23 and ADSS questionnaire to fill and after that supervised the patients who were in the experimental group in practicing diaphragmatic breathing, systematic relaxation and alternate nostril breathing while they were receiving chemotherapy.

Reminder calls were made to the participants in the experimental group once a week on every Wednesday, being mid day of the week to remind them about continuation of yoga practice.

The patients in experimental group and control group were assigned beds separately in Day Care Center, in order to prevent contamination.

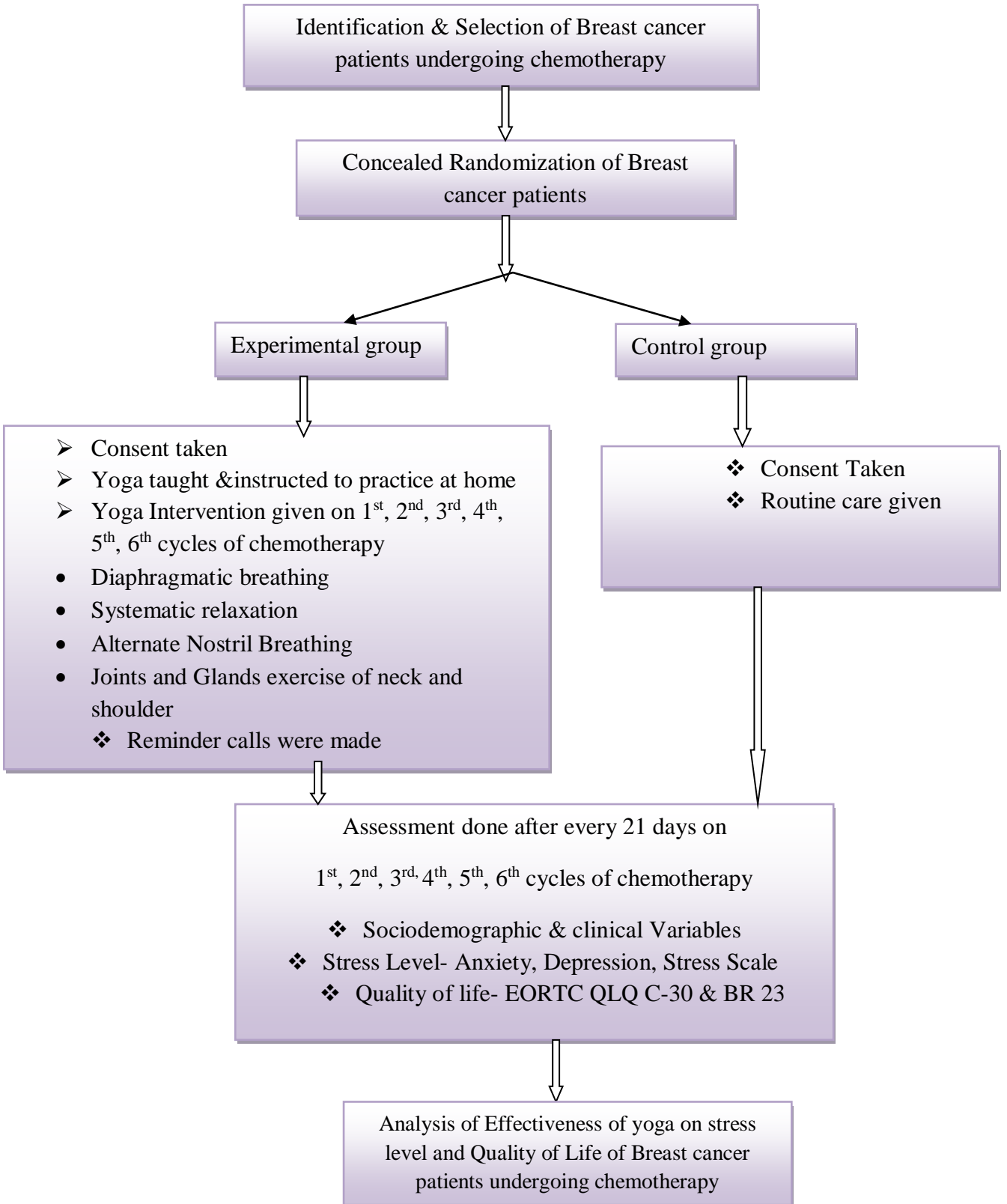
Patients in the control group received routine care which included instructions, regarding diet to be taken and care between the cycles of chemotherapy.

Routine Care: Patients in control group were given instructions regarding diet and care after chemotherapy-

- Drink adequate water in a day i.e. at least eight glasses
- Take bland diet and avoid spices and chilies in food
- Take adequate vegetables to prevent constipation
- Do not take raw fruits and vegetables
- Take home made fruit juice or tetra packed juice
- Take green vegetables
- Avoid going to crowded places
- Maintain personal hygiene
- Keep away from people having cold & cough
- Cover head with scarf

The investigator followed each of the study participants in both groups for four months throughout six cycles of chemotherapy.

Figure 6. Data collection procedure/ Study Protocol



Analysis of Data: Data was analyzed using statistical software SPSS (version 20). Categorical data expressed as frequency and percentage. Kolmogorov–Smirnov test was used to check the normality of data. Quantitative data expressed as mean \pm SD and median (minimum-maximum). Chi-square test /Fisher exact test was calculated to test the proportion between the groups. Independent “t” test was calculated to compare the statistical significance between the groups. Since variables followed skewed distribution the two groups were compared using the Mann-Whitney test. Within group effect was estimated by the Friedman test. The Wilcoxon Signed rank test was used to find the difference from the baseline score. Since, it was an experimental trial the confidence interval was estimated using independent “t” test as per the CONSORT guidelines. $P < 0.05$ was considered as statistically significant results.

All breast cancer patients recruited in the study during the first cycle of chemotherapy in both groups were included in the analysis. Patients, who discontinued chemotherapy in between second through sixth cycle, were excluded from the analysis of that chemotherapy cycle.

Summary: This chapter included type of research approach, research design, variables, setting, population, sample, sample size calculation, sampling technique, sampling criteria, description of tools, validity of tools, development of intervention, pretesting tools, ethical considerations and data collection procedure.

Figure 7. CONSORT diagram of patients' recruitment

