3. METHODOLOGY

The methodology adopted in the present study entitled “FORMULATION OF RISK INDEX AND DIET COUNSELLING FOR WOMEN WITH BREAST CANCER” was undertaken in three phases, the details of which are discussed below:

3.1 PHASE – I IDENTIFYING CONTRIBUTORY FACTORS

3.1.1 Selection of area
3.1.2 Selection of case and control subjects
3.1.3 Direct personal interview
3.1.4 Clinical assessment
3.1.5 Anthropometric measurements
3.1.6 Association between variables and breast cancer risk factors

3.2 PHASE – II FORMULATION OF BREAST CANCER RISK INDEX (BCRI) AND ASSESSMENT

3.2.1 Formulation of breast cancer risk index
3.2.2 Evaluation of formulated breast cancer risk index among selected age matched controls

3.3 PHASE – III ASSESSMENT OF NUTRITIONAL STATUS AND STRATEGY FOR PREVENTION

3.3.1 Selection of sub sample
3.3.2 Assessment of the nutritional status of selected subsamples using Patient-Generated Subjective Global Assessment (PG-SGA) tool
3.3.3 Dietary intervention and its effectiveness

3.4 HYPOTHESES OF THE STUDY

3.5 ANALYSIS AND INTERPRETATION OF DATA

The schematic presentation of research design framed for the study is given below:
RESEARCH DESIGN

Phase I
- Population sampling
  - Purposive stratified
    - Direct personal interview
      - Formulation of Breast Cancer Risk Index (BCRI)
        - Assessment of BCRI
          - Group A: Dietary intervention
            - Surgery (n = 50)
            - Radiation (n = 50)
            - Chemo (n = 30)
            - Chemo, radiation, surgery (n = 30)
            - Chemo surgery (n = 30)
          - Group B: Diet counselling only
            - Diet counselling and Supplementation
              - Outcome assessable
                * Energy and nutrient intake
                * Plasma vitamin and enzyme antioxidant
              - Diet counselling only
                - Outcome assessable
                  * Assessment of knowledge
                  * Nutritional status using scored PG-SGA tool

Phase II
- Population sampling
  - Purposive stratified
    - 1200 Women cancer
      - 914 Breast cancer
        - 800 Case subjects
          - 40-60 years
            - Treatment modality
              - Sub sample (N = 190)
                - Surgery (n = 50)
                - Radiation (n = 50)
                - Chemo (n = 30)
                - Chemo, radiation, surgery (n = 30)
                - Chemo surgery (n = 30)

Phase III
- Population sampling
  - Purposive stratified
    - 500 Asymptomatic control subjects
      - Direct personal interview
        - Formulation of Breast Cancer Risk Index (BCRI)
          - Assessment of BCRI
            - Group A: Dietary intervention
              - Surgery (n = 50)
              - Radiation (n = 50)
              - Chemo (n = 30)
              - Chemo, radiation, surgery (n = 30)
              - Chemo surgery (n = 30)
            - Group B: Diet counselling only
              - Diet counselling and Supplementation
                - Outcome assessable
                  * Energy and nutrient intake
                  * Plasma vitamin and enzyme antioxidant
                - Diet counselling only
                  - Outcome assessable
                    * Assessment of knowledge
                    * Nutritional status using scored PG-SGA tool
3.1 PHASE – I IDENTIFYING CONTRIBUTORY FACTORS

3.1.1 Selection of Area

A total of five hospitals with the Oncology Department in Coimbatore, Tamil Nadu were chosen to select the case subjects owing to its easy access and support rendered by the management of hospitals.

Among these, four private hospitals with 100 to 200 beds from Coimbatore namely, G.Kuppusamy Naidu Memorial Hospital, Ramakrishna Hospital, Ashwin Cancer Speciality Hospital and PSG Institute of Medical Science and Research and one Government Coimbatore Medical College and Hospital were selected.

Permission from higher authorities was obtained from all the selected hospitals for the conduct of study.

In order to select the control subjects the areas namely, Saibaba Colony and Ramalingam Colony situated at North Coimbatore, were selected due to easy access and familiarity of the investigator based on the convenience sampling.

3.1.2 Selection Case and Control Subjects

A universe of 1200 women between 20 and 60 years, who visited the oncology units of selected hospitals over a period of six months were interviewed to identify the type of cancer afflicting women.

The study revealed that about 914 women were suffering from the leading site of breast cancer. From these, 800 case subjects who consented to participate in the study were selected using judgment sampling technique to explore the general demographic profile and to identify the association of risk factors.

The judgment sampling is a non-probability sampling in which the sampling units are selected on the advice of some expert or by the opinion of the researcher himself (Kothari, 2008).
From the 800 women 536 subsample of case subjects were selected using stratified purposive sampling technique, based on the following inclusion criteria.

- regular follow up.
- between the age group of 40 and 60 years.
- willingness and co-operation of the participants.
- duration within 12 months at the time of the conduct of study.

Being women is the main risk factor for developing breast cancer 100 times more than men and the risk increases with the age group of above 40 years (www.cancer.gov/brisktool).

Five hundred asymptomatic women as control subjects matching the age of 40 to 60 years with the case subjects were selected by purposive stratified sampling method to stratify the highest risk for breast cancer.

3.1.3 Direct Personal Interview

3.1.3.1 Pretest

A self structured interview schedule was formulated and administered to ten selected representative sample of the study, and collected information regarding various aspects such as socio-economic status, lifestyle pattern, reproductive history, medical history and dietary pattern were pretested for consistency and accuracy. Based on the findings, the schedule were modified.

3.1.3.2 Identification of prevalence of cancer

During the six months study period the different sites of cancer prevalence were identified for 1200 women with the help of oncologist and from the self-reported data of the subjects through different follow-up contacts.
3.1.3.3 Demographic profile, environmental exposure, reproductive, medical history and dietary practices of selected case subjects with breast cancer and control subjects

The information pertaining to the study was collected at Out Patient Department (OPD) and from ward. Utmost care was taken during interrogation with women having breast cancer by not disturbing their schedule to meet oncologist or when waiting for the treatment purposes. Participants who willingly provided the information were solicited and others who felt embarrassed or had social stigma were excluded from the survey.

**Demographic Profile**

Using a well framed pretested interview schedule as shown in Appendix-I, the details regarding age, area of residence, educational status, occupation, economic status, marital status and type of family were collected from selected 800 case subjects and 500 age matched controls (Plate 1).

**Life style pattern**

Life style factors included habit of chewing tobacco, betel leaves, paan, type of activity, sleep pattern, mode of transport and exercise pattern and the information on these factors were elicited from the selected subjects.

**Environmental Exposure**

Type and frequency of chemicals handled personally at home and at work spot, and use of mosquito repellents were studied.

**Reproductive Factors**

Regarding the reproductive history, all the subjects were interviewed about age at menarche, duration and regularity of menstrual cycle, adjustment in menstrual cycle, age at marriage, age at first child birth, use of contraceptives, gynaecological complications, mode of delivery, breast feeding practices, menopausal age, symptoms and complications during menopause.
Medical History

Information regarding diagnosis method, time of detection, symptoms noted, treatment undergone, consequences and discomfort experienced by selected case subjects were collected as a part of medical history.

Dietary Practices

In the dietary practices, the type of diet, consumption pattern of non-vegetarian foods, methods of cooking adopted, type of oil used for cooking, habit of using reheated oils, type of beverages consumed, use of preservatives, preference for soft drinks, and items consumed at food service outlets were elicited from all the subjects.

3.1.4 Clinical Assessment

Clinical examination was done for 800 case subjects using schedule shown in Appendix II to find out the clinical signs and symptoms and to associate it with the specific nutrient deficiency or excess intake.

It is based on examination for changes, related to inadequate nutrition, that can be seen or felt in superficial epithelial tissues, especially the skin, eyes, hair or in organs near the surface of body (Jelliffe, 1989).

3.1.5 Anthropometric Measurements

Anthropometry is the science of measuring the size, weight, height and the proportion of human body and is the most commonly used direct method for the assessment of nutritional status in all age groups (Jelliffe, 1989).

Height and weight were measured using standard methods for all 800 case subjects and 500 controls.

Height

The height of an individual is principally a measure of skeletal body tissue, legs, pelvis, spine and skull (Jelliffe, 1989). The subjects were allowed
to stand straight on a flat floor against the wall without foot wear. They were made to stand such that their head, back, shoulder, buttocks and heels touched the wall and their head erect. A horizontal scale was gently placed over the head of the subjects without pressing and a mark was made on the wall. Distance between the position of head and toe was measured using the non-stretchable fibre glass measuring tape and the height was recorded for all subjects to the nearest accuracy of 0.1 cm.

**Weight**

The weight of the subjects was measured using the bathroom scale in the morning with ordinary light clothes and after removing their footwear. The weight was recorded to the nearest accuracy of 0.5 kg.

**Body Mass Index (BMI)**

The most widely used clinical tool for measurement of malnutrition and obesity is BMI, calculated using the formula,

\[
\text{Body Mass Index} = \frac{\text{Weight (kg)}}{\text{Height (m}^2\text{)}}
\]

(National Institute of Health, 2000).

BMI was computed for all subjects and were grouped based on BMI classification (WHO, 2007) as given below:

<table>
<thead>
<tr>
<th>BMI</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>Chronic Energy Deficiency (CED) III</td>
</tr>
<tr>
<td>16 – 17</td>
<td>CED II</td>
</tr>
<tr>
<td>17 - 18.5</td>
<td>CED I</td>
</tr>
<tr>
<td>18.5 - 20</td>
<td>Low weight</td>
</tr>
<tr>
<td>20 - 25</td>
<td>Normal</td>
</tr>
<tr>
<td>25 – 30</td>
<td>Obesity Grade I</td>
</tr>
<tr>
<td>&gt; 30</td>
<td>Obesity Grade II</td>
</tr>
</tbody>
</table>
3.1.6 Association Between Variables and Breast Cancer Risk Factors

Using SPSS version 15.0 the association between the selected variables and the breast cancer risk factors were analyzed by factor analysis.

3.2 PHASE – II FORMULATION OF BREAST CANCER RISK INDEX (BCRI) AND ASSESSMENT

3.2.1 Formulation of Breast Cancer Risk Index

As most work defining risk factor has centered on old women (Tavani et al., 1999), 536 case subjects between 40 and 60 years of age were selected as that of age matched control group of 500 asymptomatic women population for the formulation of cancer risk index.

Based on Gail model the factors were scored using SPSS package version 15.0 to find out the order of risk factor and to formulate a risk index.

In all subjects, a structured questionnaire was administered which includes details on current age, education level, occupational status, income, area of residence, marital status, body mass index, menarchial age, regularity of menstrual cycle, age at marriage, age at first child birth, parity, duration of breast feeding, use of contraceptives, menopausal age, tobacco chewing habit, usage of chemicals as disinfectant, type of diet, meat consumption, use of reheated oil and use of artificial food colours. Univariate regression analysis was performed using newly detected cancer as the dependent variable and various possible risk factors as independent variables. Those variables which were found to be significantly associated with cancer in univariate regression analysis were included in the multiple logistic regression analysis. Thus, multiple logistic regression analysis was done using newly detected cancer as the dependent variable and the various risk factors such as age at menarche, regularity of menstrual cycle, age at first child birth, meat consumption and use of chemicals as independent variables to obtain the risk scores. Based on the beta co-efficients, a score was created for each parameter. The simplified Breast Cancer Risk Index (BCRI) was then determined by adding the scores
for each risk factor. The specificity of the index was validated by Receiver Operating Characteristic (ROC) curve.

### 3.2.2 Evaluation of Formulated Breast Cancer Risk Index Among Selected Age Matched Controls

The higher incidence of breast cancer among women in Coimbatore, was found to be between 45 and 54 years as per Cancer Atlas India Registries (www.canceratlas.India).

Hence the derived Breast Cancer Risk Index was applied to controls to assess the risk. The degree of risk generated from the ROC curve (≥ 13) as a risk score, was used to identify the control subjects at risk and not at risk.

The simplified Breast Cancer Risk Index (BCRI) will be a tool to detect the probability of breast cancer among asymptomatic population.

### 3.3 PHASE – III ASSESSMENT OF NUTRITIONAL STATUS AND STRATEGY FOR PREVENTION

#### 3.3.1 Selection of Subsample

Among 536 breast cancer women a subsample of 190 subjects visiting clinics regularly for follow up and who rendered full co-operation were selected after obtaining ethical consideration for Phase III of the study by stratified purposive sampling.

Based on the different treatment modality they were divided into two groups, comprising 100 and 90 case subjects in Group A and Group B respectively.

<table>
<thead>
<tr>
<th></th>
<th>Treatment modality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group A</strong></td>
<td></td>
</tr>
<tr>
<td>I (N= 50)</td>
<td>Surgery</td>
</tr>
<tr>
<td>II (N= 50)</td>
<td>Radiation therapy</td>
</tr>
<tr>
<td><strong>Group B</strong></td>
<td></td>
</tr>
<tr>
<td>III (N= 30)</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>IV (N=30)</td>
<td>Combination of chemo, radiation and surgery</td>
</tr>
<tr>
<td>V (N=30)</td>
<td>Combination of chemo surgery</td>
</tr>
</tbody>
</table>
3.3.2 Assessment of the Nutritional Status of Selected Subsamples Using Patient-Generated Subjective Global Assessment (PG-SGA) Tool

The nutritional status of 190 subjects in Group A and B were assessed using Patient-Generated Subjective Global Assessment (PG-SGA) tool.

The Patient Generated-Subjective Global Assessment (PG-SGA) tool which was developed specially for patients with cancer (Ottery, 1994) is shown in Appendix III. It includes additional questions regarding the presence of nutritional symptoms and short-term weight loss, along with medical history and the details of physical examination. The components of medical history can be completed by patient using a check box format. The physical examination was performed by health professional, e.g., physician, nurse or dietitian.

The scored PG-SGA is a further development of the PG-SGA concept that incorporated a numerical score as well as providing a global rating of well-nourished, moderately or suspected of being malnourished or severely malnourished. Each component of the scored PG-SGA, points (0-4) were awarded depending on the impact of the symptom on nutritional status. A total score was then summed and this provides a guideline as to the level of nutrition intervention required, as well as facilitating quantitative outcome data collection (Ottery, 2000). The scored PG-SGA, unlike SGA, which is categorical, is a continuous measure. The higher the score the greater the risk for malnutrition. A score $> 9$ indicates a critical need for nutrition intervention.

Nutrition triage recommendations include patient and family education, symptom management and nutrition intervention such as additional food, oral nutrition, supplements, enteral or parenteral nutrition. The scored PG-SGA has been accepted by the oncology Nutrition Dietetic Practice Group of the American Dietetic Association as the standard for nutrition assessment among cancer subjects (Bauer et al., 2002).
The tool was adopted before and after specific dietary interventions to
the groups as a part of assessing the nutritional status.

3.3.3 Dietary Intervention and its Effectiveness

Ethical consideration

Approval from the Institutional Human Ethics Committee from the PSG
Institute of Medical Science and Research, Coimbatore was obtained in order
to carry out the dietary intervention (Appendix IV).

Oral consent was obtained from the selected 190 subsamples who
were willing to participate in the study. Regular contact and observation was
maintained. The intervention given to women undergoing different treatment
modalities is shown below:

<table>
<thead>
<tr>
<th>Groups</th>
<th>Intervention and Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (surgery + radiation) (N=100)</td>
<td>PGSGA – assessment, diet counselling, supplementation of antioxidant rich food.</td>
</tr>
<tr>
<td>Group B (combination of treatments) (N=90)</td>
<td>PGSGA – assessment, diet counselling, without supplementation of anti-oxidant rich food.</td>
</tr>
</tbody>
</table>

Effectiveness of dietary intervention (Plate 1) was assessed after 12
weeks in terms of knowledge gained and nutritional status using PGSGA tool.

3.3.3.1 Diet counselling to selected subsamples

Despite a wealth of scientific data, most people remain unaware of how
they can reduce the risk of developing cancer.

Diet counselling plays an important role in motivating individual in the
development of healthy habits and attitudes (Venkatiah, 2000). Nutritional
counselling offers a great opportunity to individuals to learn about the
essentials of nutrition for health and to take steps to improve the quality of
their diets and thus their well being (Robinson, 2004).

Nutrition can play an important role in the management of
the cancer patient, across the spectrum from the initial phases of treatment
and recovery through the long-term continuum of care in which the goals are
to prevent recurrence, to reduce risk for comorbid disease, and to increase
likelihood of survival. Individuals who have been diagnosed with cancer are often motivated to modify their diets and seek nutritional guidance (Brown et al., 2003). Food choices and eating patterns are one aspect of life over which the patient has some control, and these are modifiable factors.

Evidence from the study by Ravasco et al. (2005), suggest that individualized dietary counselling can be successful in enabling patients at high risk of deterioration in nutritional status to maintain good status, which is accompanied by a reduction in symptoms and improved health-related quality of life.

For breast cancer survivors, the focus of dietary and lifestyle intervention is generally to promote healthy weight management and a moderate rate of weight loss in the overweight or obese patient through modified intakes and increased physical activity (Rock and Wahnefried, 2002). Whether dietary counselling in other target groups across the cancer continuum can alter outcomes (Pierce et al., 2004), and continued research efforts in this area are anticipated.

Hence diet counselling was given to 190 women with breast cancer undergoing different treatment modalities, using booklets, pamphlets and posters for a period of 12 weeks duration during their schedule of visiting oncologist for the treatment purpose.

Booklets and pamphlets as shown in Appendix V with details of nature of the disease, diagnosis and treatment to be followed at early stage of cancer detection and significance of preventive measures were developed in English and in regional language Tamil and were distributed to all selected subsamples.

Using lecture method the details regarding breast cancer, signs and symptoms, need for early detection, method of self-examination, clinical breast examination, different treatment available for breast cancer, possible consequences due to treatment and the dietary recommendations to overcome were imparted to the subjects in groups every month, fortnightly during their schedule visit for treatment.
Individual counselling as well as group counselling was carried out using pamphlets and exhibits and individual queries were answered during counselling session for a period of 12 weeks on rotation basis to the subjects depending upon the treatment methods received at the hospital.

The impact of counselling among selected 190 subsamples on the knowledge gained was assessed after 12 weeks using a check list as shown in Appendix VI and by designed software assigning scores. A software was developed (Appendix VII) using dot net, to impart and assess the knowledge related to cancer. The software consists of knowledge test covering different aspects of breast cancer and diet. Questions with and without scores was designed to create awareness on breast cancer as well as to familiarize with the skill to operate the software product. The scores ranged from (1-3), (4-6), (7-9) labelled as poor, fair and good respectively for each question.

3.3.3.2 Supplementation of antioxidant food to selected subsamples

The relationship of nutrition and breast cancer has been a subject of much research since 1970's. Despite the plethora of articles, no strong conclusions can be made with regard to the association of nutrition and breast cancer.

Fruits, vegetables and antioxidants intake around the time of breast cancer diagnosis may be associated with an improved prognosis. Several studies have suggested that intake of these food items may prolong survival (Ziegler, 1991 and Byers and Gvererro, 1995).

Components of fruits and vegetables have demonstrated the ability to inhibit breast tumour cell proliferation in cell culture and animal studies (Zhang et al., 2005 and Kano et al., 2005). Carotenoids rich in fruits and vegetables have demonstrated similar effects through induction of apoptosis and inhibition of mammary cell proliferation (Prakash et al., 2000).

Group A, was supplied with 100 g carrots every week when visited oncology units for treatments and follow-up if not visited supplied through their attenders.
The subjects used carrots either in the form of porriyal* or raw juice. Regular follow-up visits and telephonic contacts were maintained during the study period.

* Porriyal is a traditional accompaniment for main dish in South Indian menu. Carrots were cut into small pieces or shredded. It was seasoned and cooked well for 10-15 minutes without leaching the water added. The taste was enhanced with salt and dressed with coriander leaves or grated coconut as options.

In order to assess the impact of antioxidant supplement 13 case subjects who cooperated were studied thoroughly for further follow-up studies. Due to limitations, six case subjects were included in the study.

The effectiveness of supplementation after 12 weeks among selected six subsamples with various treatment modality was assessed by estimating plasma vitamin antioxidant-β carotene, vitamin C, vitamin E and haemoglobin using standard procedures (Appendix VIII) of Kimble (1939), Omaye et al. (1971), Baker and Frank (1968) and the cyanmethaemoglobin method respectively, and the enzymatic antioxidant status such as glutathione peroxidase (Rotruck et al., 1984) and superoxide dismutase (Mishra and Fridovich, 1972).

Limitations

- Among 13 subjects four subjects had recurrence of secondary and were unable to follow-up. Due to the termination of life of one case subject and two dropouts for unknown reasons the case subjects were restricted to six for the impact study.

- Cost factor of estimation in biochemical parameters such as plasma vitamin and enzymatic antioxidant level and shortage of time to continue further, were the other limitations.
PLATE 1
ELICITING BACKGROUND INFORMATION OF SELECTED WOMEN
3.4 HYPOTHESES OF THE STUDY

H₁ Socio economic status, reproductive factors, chemical use and dietary pattern are the major risk factors leading to breast cancer among women.

H₂ Diet counselling significantly improves the knowledge of case subjects

H₃ There is an association between PGSGA score and dietary intervention.

H₄ Diet counselling improves the energy and nutrient intake of the selected breast cancer cases.

H₅ Supplementation of antioxidant rich food shows positive impact on plasma vitamin and enzymatic antioxidant levels among selected breast cancer cases.

3.5 ANALYSIS AND INTERPRETATION OF DATA

SPSS Statistical package version 15.0 was used to carry out all the necessary analysis.

• Chi-square test was applied to test the difference in demographic factors and reproductive factors among cases and control subjects.

• In order to identify the contributory risk among the case subjects, factor analysis was carried out. Factor analysis is a form of multivariate analysis that takes a large number of variables or objects and aims to identify a small number of factors that explain the interrelations among the variables or objects. (www.esomar.org/index.php/glossary-f.html).

• Multiple logistic regression is an accepted statistical method for assessing association between an antecedent characteristic (risk factor) and a quantal outcome (probability of disease occurrence), statistically adjusting for potential confounding effects of other covariates (Lee, 1986). Multiple logistic regression analysis was done using newly detected cancer as the dependent variable and the various risk factors as independent variables.
to obtain the risk scores. Based on the beta co-efficients, a score was created for each parameter. The simplified Breast Cancer Risk Index (CRI) was then determined by adding the scores for each risk factor.

- Correlation matrix and one way Analysis of Variance (ANOVA) done were to associate the PG-SGA score and dietary interventions of selected subsamples.
- Chi-square test was carried out to associate the knowledge of cancer in relation to variables such as educational level, income and age of the case subjects.
- Students ‘t’ test was applied to observe the significant impact of dietary intervention.