CHAPTER 5

SUMMARY, FINDINGS, DISCUSSIONS AND CONCLUSIONS

This chapter presents the summary, findings and discussion of the study and conclusions. It also includes the implications, limitations of the study and suggests recommendations for further research.

5.1. Summary of Study

The main aim of the study was to explore the outcomes of pharmacological management of women with breast cancer in a tertiary care centre of Udupi district of Karnataka, India.

The specific objectives of the study were:

1. To identify and describe the pattern of pharmacological management among women with breast cancer in the centre.

2. To identify the treatment associated economic outcome of pharmacological management of women with breast cancer

3. To identify the clinical outcome of pharmacological management of women with breast cancer by examining the predictors of survival of these women.

4. To identify the predictors of adherence to treatment by the women with breast cancer

5. To compare the humanistic outcomes amongst the different pharmacological treatments of women with breast cancer.

The null hypotheses of the study were:

H₀₁: There will be no significant differences in the economic outcome when
different pharmacological treatment regimens are adopted for treating women with breast cancer.

\( H_02: \) There will be no significant differences in the survival pattern among women with breast cancer when different pharmacological treatments are adopted.

\( H_03: \) There will be no significant differences in humanistic outcomes when different pharmacological treatment regimens are adopted at different stages of breast cancer.

Theoretical basis for this outcome study was developed based on two conceptual frameworks, the modified ECHO planning model for pharmaco-economic outcome research and Aday-Anderson model for determinants of health care utilization behavior.

The survey approach was used for this comparative descriptive study. Women with breast cancer receiving treatments and/or follow-ups were the subjects considered for inclusion in the study. The sample size was 303. A purposive sampling technique was used to collect required information. The data was obtained by using a background proforma, including demographic details, disease characteristics and treatment variables. The questionnaire used for measuring the humanistic outcomes comprised of EORTC QLQ C 30 and its breast specific module QLQ BR 23. The content validity of the developed proforma was established by experts and the reliability was established by Cronbach’s alpha for EORTC QLQ C 30 and QLQ BR 23. (\( \alpha = 0.76 \)).

A pilot study was conducted with 27 patients before starting the main study to determine the feasibility and practicality. The study was conducted in wards and day care centre of Shirdi Sai Baba Cancer Hospital and Research Centre, Manipal, India 576104. The independent variables were different pharmacological treatment regimen prescribed for breast cancer patients, stage of cancer at diagnosis, distant and nodal metastasis at the time of diagnosis, disease grade, hormone responsiveness and duration of illness. The dependent
variables were pharmacological treatment related economic outcome, clinical outcome, humanistic outcomes and adherence to treatment. Age, family income, education, employment and marital status were considered as extraneous variables in this study.

The data collected were analyzed based on objectives using statistical software package for social sciences, SPSS version 11.5. Both descriptive and inferential statistics were used to interpret the results. Frequency and percentage were used to describe sample characteristics, disease and treatment variables.

A total of 303 women with breast cancer, who were receiving treatment in Shirdi Sai Baba cancer Hospital and Research Centre, Manipal were invited to participate in the study after getting informed consent. The age of participants varied from 25-73 years, (mean age 47.23, SD=9.7). Out of 303 women, 53% were premenopausal and the rest of them were post menopausal. From 303 subjects studied 274 (90.4%) were married and cohabiting with their spouses and others were unmarried, widowed or separated. The economic background was categorized into 3 classes as low income group (INR<5000/M), middle income group (INR-5000-10000/M) and high income group (INR >10000/M). The distribution of socio-economic status was low for 50.8% subjects, medium for 34% and high for 15.2 % of subjects. The educational qualification ranged from primary education and less 32.4%, 50.5% with 5th -10th class and 16.9 % college education. The stage wise distribution of breast cancer was stage I (2.6%), stage II (39.6%), stage III (39.6%) and stage IV (14.9%). Hormone responsiveness of tumors was found to be 57% as ER +ve. Majority, 93.7% of them had surgical intervention, out of which 70.9% underwent Breast conserving surgery, 7.2% had mastectomy, 8.6% had lumpectomy and others had minor surgical procedures. Surgical interventions were supplemented with radiation therapy to chest wall.

Out of 303 women, 81.5% were supplemented with chemotherapy by different drug regimens. All the ER/PR+ve cases were prescribed with tamoxifen /aromatase inhibitors for 5 years after the preliminary treatments, according to the menopausal status.
Chemotherapy with AC drug regimen (regimen I; Adriamycin (60 mg/m$^2$) and cyclophosphamide (600 mg/m$^2$)) was used for treating 26.7% of subjects. Subjects diagnosed at metastatic stage (16.8%) were treated with 6 cycles of 5 Fluorouracil (600 mg/m$^2$), Adriamycin and cyclophosphamide (FAC, regimen II). Another group, 47.2% who reported in advanced stages of the disease, were treated with 8 cycles (ACx4 + Taxol x 4 (60-75 mg/m$^2$/kg) (ACT, regimen III).

The treatment related economic outcome was calculated in Indian rupees as costs of consultation, drugs, investigation, surgical treatment, radiotherapy, professional and service charges and as total direct cost. The mean direct costs of treatment for the 3 regimens were INR 114929, 133073 and 177037 for regimen I, II and III respectively. The costs per each QALY were estimated as INR 11897, 42789 and 285543 for regimens I, II and III respectively. Kaplan Meier survival analysis was carried out and found the survival rate as 11.01, 2.52 and 1.10 years mean survival for regimens I, II and III. Cox proportional hazards regression analysis was carried out and identified the predictors of survival of breast cancer patients as the stage of disease at diagnosis and adherence to treatment. Logistic regression analysis revealed that spouses support and the distant metastasis at diagnosis as the predictors of adherence to treatment. The humanistic outcome was described as mean and standard deviation as different domains of functional scores and different symptoms experienced after treatment. Regimen III patients had best humanistic outcomes among the three in terms of functional scales and symptoms scores and regimen II patients had the worst humanistic outcomes. One way ANOVA was conducted to compare the means of humanistic outcomes among different treatment groups. The results showed that there were significant differences in the humanistic outcomes in few functional scores and symptoms scores of quality of life. The significant scores in the quality of life in functional aspects were Physical, role, emotional functions and global health (P=< 0.05). The symptoms scores which gave significant p values were pain, constipation and upset by hair loss. Post hoc analysis for multiple comparisons revealed that there are slight differences.
in quality of life after chemotherapy between regimen II and regimen III patients.

5.2. Major Findings of the Study and Discussions

5.2.1 Sample characteristics

The age of study participants ranged from 25 to 73 years, (mean age 47.23, SD=9.7). Pakseresht et al had reported that the mean age among breast cancer patients studied for expenditure audit was 46.99(SD=12.64).\(^6\) Sandu et al reported that out of 304 patients studied, the mean age was 47.39% (SD=10.90). The present finding is in conformity with many other studies in India, except a minor variation in the figures. However this age is almost 10 years less than that of the west.\(^6\) Thomas et al reported that in general the biology of the disease is more influenced by age.\(^\text{13}\) The more young women were diagnosed with breast cancer, was presented with aggressive, often ER negative disease. In contrast, elderly women present with less aggressive, ER positive disease. In agreement with the above report the present study also revealed that there was a positive correlation between age and estrogen receptor status (r = .132, P=0.026). However, the analysis by specific age group showed an equal distribution of ER negative and positive tumors in elderly women (age 60 years & above). In contrast 68.6% of the younger women (< 40 years) had ER positive disease. In the middle age group (41-59 years) 66.2% had ER positive tumors. At the same time lymph node involvement was maximum (78.5%) in younger women, followed by 73.7% in elderly women. The middle age group (41-59 years) had 66.2% ER/PR positive tumors and 33.8% ER/PR negative tumors.

The menopausal status of the subjects was observed as 53% premenopausal and 47% post menopausal. The marital status of subjects was denoted as 90.4% married and cohabiting with their spouses and others widowed or separated. The economic background was categorized in to 3 classes as low (INR<5000/M), middle (INR-5001-10000/M) and high (INR >10000/M). The distribution of subjects was 50.8% from low income families, 34% from middle income families...
and 15.2 % from high income families. The educational background ranged from primary and less to the tune of 32.4%, secondary school education for 50.5% and 16.9 % college education.

5.2.2 Disease characteristics

The stage wise distribution of breast cancer varied from stage I (2.6%), stage II (39.6%), stage III (39.6%) and stage IV (14.9%). Fifty four point two percent of the group had advanced stage of cancer (stage III and IV) and 42.8% was in the initial stage (stage I and II) of breast cancer. Only 16.2% of subjects reported the disease and sought treatment in the hospital in less than 1 month, 54.4% of subjects reported to hospitals 2-6 months of disease signs and 13.2% of them reported after 6 months after noticing disease signs.

Infiltrating ductal carcinoma was observed in 93.3% of subjects. Out of 303 women, 80.9% had no co morbidity and others had co morbid conditions like hypertension, diabetes mellitus and others. The hormone responsiveness was positive(ER+ve/PR+ve) for 57.1% of subjects and 51.2% of them had HER2 +ve (Human Epidermal Growth Receptor+ve) tumors. Lymph node metastasis was observed in 65% of subjects at varying degrees at the time of diagnosis. Lump size was less than 2cm in 16 subjects, 215 had lump size 2 to 5cm and 69 subjects had lumps more than 5cm.

Litton et al conducted a study to find the relationship between obesity and pathological response to neoadjuvant chemotherapy among women with operable breast cancer at Anderson cancer centre and found that BMI was associated with worse pathological complete response. In the present study there was not much correlations between BMI and disease free survival (r=-0.001, p=0.98).However, obesity, as measured using BMI is generally regarded as a poor prognostic factor for breast cancer and it should be a warning message to all breast cancer survivors. It has been proposed that obesity influences breast cancer prognosis by increasing circulating plasma levels of estrogen, insulin, insulin like growth
factor and the hormonal factors that act to promote the growth of occult metastatic disease.\textsuperscript{67}

Borgquist et al conducted a study to find the association of anthropometric factors with post menopausal breast cancer. Six anthropometric factors; height, weight, BMI, waist and hip circumference and body fat percentage, were categorized as quartiles of baseline anthropometric measures and relative risks were calculated using multivariate Cox regression models. Women in the highest quartiles of weight, BMI, waist and hip circumference and body fat percentage were all associated with tumors of ductal type, grade II, HER 2 negativity and low expression of oncogenes cyclin D1. This study confirmed association between obesity and post menopausal breast cancer.\textsuperscript{68}

Many patients reported the disease after many months of noticing early signs of disease. Delay in diagnosis and treatment will reduce survival. Conducting awareness programme on breast and other cancers, focusing on important signs and symptoms of different cancers can lead to early detection of different cancers, by means of early reporting and biopsies. This can reduce cancer mortality and disease free survival. In the present study, out of 303 women, only one case was detected by screening mammography. All other cases were detected by the patients by themselves with early signs such as breast lumps, unhealed breast ulcers, and nipple discharges. This suggests for the need for conducting awareness programs among the women. Regarding awareness of hereditary cancers, awareness programmes are necessary. Educating women about such risk factors will be beneficial for early detection and treatment.

Somadata and Baridalyn conducted a study among an urban resettlement colony (n=333) in Delhi and found that the women in that colony had poor knowledge about breast cancer risk factors, warning signs or early detection procedures. Only 56% of the women had awareness of breast cancer and only 35% of the group knew few details about risk factors.\textsuperscript{69}. They opined that it is important to create awareness and educate the community and to remove the misconceptions and myths associated with ignorance through community based educational
campaigns. Early warning signs and significance of a painless lump need to be emphasized. In the present study, 99% of the group had come forward to seek medical assistance for the diagnosis and treatment voluntarily. This is a positive sign that women are watchful of this disease. However awareness is required to report the disease, at an early stage, which is very important in improved disease free survival.

Atoum et al conducted a study among the Jordanian females aiming at pinpointing the frequency of each stage among the familial and non familial breast cancers including ninety nine women during the year 2000-2002 and found that 43 cases were familial breast 56 were non familial breast cancers. The study concluded that the incidence of non familial breast cancer were slightly higher than that of familial breast cancer among the Jordanian women studied. The occurrence of familial breast cancers are comparatively less, when compared to non familial breast cancers. However, as per the opinions from experts, it is advisable to be on watch by those women, who have close blood relatives with breast cancer. According to the background information obtained, the present study also found that the occurrence of familial breast cancer is very minimal (1.65%). More than 65% of the patients had lymph node metastasis at varying degrees. A negative correlation was found between duration of symptoms at reporting to start the treatment and survival (r=-0.143, p=0.02). Conducting awareness programs can be helpful for those women to report the disease at the earliest and seek treatment for better survival.

5.2.3. Pharmacological and other treatment variables

Surgical management is considered the primary important procedure in management of breast cancer, which can be operated. Even among women presenting with stage IV breast cancer, 35-60% undergoes local therapy, presumably to avoid uncontrolled chest wall disease. Several studies suggests that resection of the primary tumor prolong survival. In the present study, 93.7% subjects had surgical intervention, out of which 70.9% underwent
breast conserving surgery (modified radical mastectomy), 7.2% had mastectomy, 8.6% had lumpectomy and others had minor surgical procedures. Surgical treatment was supplemented with radiation therapy to chest wall. For women diagnosed with early-stage breast cancer, lumpectomy followed by radiation therapy has been shown to be as effective as mastectomy without radiation for removing the cancer and minimizing the risk of recurrence. Adjuvant radiation therapy can destroy any cancer cells that may have been left behind after surgery, making recurrence less likely and also improve overall survival. In a meta-analysis carried out with 17 studies on the benefits of adjuvant radiation therapy after lumpectomy involving more than 10,000 women; the studies compared the outcomes of women who got adjuvant radiation therapy to women who didn't. In the 10 years period after surgery: 19.3% of women who got adjuvant radiation therapy had a cancer recurrence and 35% of women who didn't get radiation therapy had a recurrence. The results also strongly support doctors' current understanding that lumpectomy followed by radiation therapy is a very good alternative to mastectomy for many patients.72

Out of 303 women, 81.5% were supplemented with chemotherapy by different drug regimens. All the hormone responsive cases were prescribed with tamoxifen / aromatase inhibitors for 5 years following the preliminary treatments, with chemo and/or radiations, according to the menopausal status. Three drug regimens were popularly employed for breast cancer management in the study center. Regimen I [(AC x 4 cycles regimen; adriamycin (60mg/m²) and cyclophosphamide (600mg/m²))] was used for treating 26.7% of subjects, regimen II [(FAC x 6 cycles regimen; 5 Fluorouracil (600mg/m²), adriamycin and cyclophosphamide)] in 16.8% of subjects and regimen III [(AC+Taxol 8 cycles; (60-75mg/m²/kg)] in 47.2% of subjects.

Locally advanced breast cancer, which accounts for 30-35% of all cases in India, poses a challenge for care givers. Survival rates for locally advanced breast cancer may vary according to the different treatment options adopted. There may be institutional differences in therapeutic policies. Overall results of
the treatment of this subset of breast cancer are miserable. A long term survival is expected for not more than 30-40% of this group. Advanced stage breast cancer and poor results of treatment represent a major public health problem of our country.

Kristie et al conducted a study among Medicaid-insured breast cancer patients treated with breast conserving surgery with and without radiation treatment and found that the adjuvant radiation following breast conserving surgery, will improve survival rate of breast cancer patients.

Comparative trials in both the metastatic and adjuvant settings have shown that the anthracycline containing regimes are more effective, achieving consistently higher response rate, longer time to progression and improved survival rates. More recently anthracycline and taxanes containing regimens have proven to be more effective than AC or FAC in several randomized trials. Addition of taxanes with conventional anthracycline containing regimens is considered the new standard of care in node positive patients. Dose dense therapy, the administration of drugs with a shorter interval in adjuvant setting has resulted in statistically significant improvement in disease free and overall survival.

The amplification and over expression of the Epidermal Growth Factor Receptor family of receptor tyrosine kinases, commonly referred to as HER2 in human breast cancer has been associated with poor prognosis. Since its initial discovery in 1986, HER-2 was intensively researched as a therapeutic agent and trastuzumab has marked the culmination of that search. Its incorporation as a component of adjuvant therapy in HER-2 positive tumors has been shown to improve disease free and overall survival. In the present study 2.9% of subjects, who had over expression of HER 2 protein in their tumors were treated with trastuzumab (Herceptin). Although, many of the patients were prospect candidates for herceptin treatment, very few could opt for it, mainly because of financial constraints.
All cases with hormone responsive tumors (57.1%) were prescribed with adjuvant hormone therapy for 5 years as a preventive measure from recurrence. Tamoxifen (70.5%) was the main drug used for adjuvant hormone therapy in the premenopausal women and letrozole (27.7%) or anastrozole (1.7%) in the postmenopausal women. Majority of the risk factors for breast cancer are hormone related. Based on this fact, approaches to breast cancer prevention should focus on reducing women’s lifetime exposure to endogenous ovarian hormones. Unfortunately, most of the hormonal risk factors are not modifiable. At present the only risk factors amenable to modifications are postmenopausal obesity, alcohol consumption, improving physical activity and restricting hormone replacement therapy.\textsuperscript{75,76}

5.2.4. Pharmacological treatment related economic outcome

The treatment related economic outcome for all 3 treatment groups was calculated in INR as costs of consultation, investigations, drugs, surgical treatment, radiotherapy, professional and service charges and total direct cost to evaluate the economic outcome of different treatments. The cost evaluation revealed that total treatment cost was in the increasing order (INR 114929/-, INR 133073/- and INR 177037/- for regimens I, II, and III respectively). The cost of drugs in regimen III was 45.5% of the total direct cost where as, the cost of drugs was 26% and 31.2% of total costs for regimen I and regimen II respectively.

The major differences in cost among these treatment regimens were due to the cost differences of drugs. All other costs did not make much differences among the three, except in those charges incurred due to complications or if opted for special private ward care. In addition to these direct medical costs, patients had some other indirect costs due to the sickness, which is not accounted here. The other expenses met by the patients include, cost of travelling for self and attendants, rentals for room for persons accompanying, dietary expenses for patient as well as the attendants, salary lost by the employed persons (patients
and the attending persons) , and salary paid if any persons were employed to take care of the patient/household works. Also the intangible costs, due to the pain and agony a patient and the family undertake after breast cancer diagnosis need to be considered in pharmacoeconomic evaluations. All these costs make indirect costs of treatment of breast cancer. In this study only direct medical expenses are included and no attempt is done to calculate the indirect costs, which is limitation of this pharmacoeconomic study.

The cost per each year of quality adjusted life year (QALY) for the 3 treatment regimens was computed by multiplying mean survival with overall quality of life score and then dividing the value with the mean cost of respective groups. The cost per each QALY for the 3 treatment regimens, was identified as INR-11897/-, INR 42789/- and for INR- 285543/- for regimens I, II and III respectively. Here the cost per each QALY seems to be very less for patients in regimen I when compared with those in regimens II and III. But these are not a comparable group as these regimens are not equal alternatives with equal expected outcomes. Drug regimen I is mainly used when the disease is in its early stages, when lymph nodes are not involved, where as FAC and ACT regimens are prescribed when the disease is in the advanced stages. If we consider II and III drug regimens, there was a huge difference in cost per each quality adjusted life year (QALY). Based on the cost and effects (survival and patient reported humanistic outcomes), there were significant differences in cost per QALY between treatment regimen II and III. In terms of patient reported humanistic outcomes regimen III patients were found to be better, because all domains of functional scores except future perspectives were higher in regimen III and the symptoms and unwanted effects except constipation was found lesser. But the cost per QALY is very high (INR 285543/-) when compared to the cost per QALY for regimen II (INR 42789/-). It is up to the decision makers, both the physicians and the patients to make choice among the two treatments.

The country offers a wide variety of health care services to its population. On one side there are advanced hospitals and diagnostic centers in urban areas,
where as the rural population largely depend on government hospitals and health centers for health care services. In the middle of these 2 extremes there are private hospitals, private practitioners and clinics. Despite health being a major concern of the government, the majority of India’s health infrastructure is in the private sector and more than 70% of health care expenses are met by the consumers out of their pocket. To address healthcare affordability, commercial health insurance was introduced in the country by the government owned general insurers as a standardized annual indemnity product, for assuring better access for quality healthcare. At present with increased liberalization of the insurance industry, many private players have entered the insurance market resulting in increased awareness and growth of commercial health insurance. Currently around 20% of the total population is covered under health insurance schemes, with majority covered under either government or employer programs. Regular health insurance has less than 2% penetration.\(^7\)

The present study finding showed that only 9.9% of the subjects were receiving full financial support for direct medical costs. Another 15.5% of subjects were receiving partial financial support from different agencies and/or charitable trusts. A good majority, 67.9% were spending out of their pocket. Health insurers in India currently face many challenges, including poor consumer awareness, strict regulations, and inefficient business practices. They operate under a combination of high administrative costs and medical expense ratios which have ensured that insurers operate under steep losses. To overcome these challenges, health insurers need to innovate in their product offerings and tighten their existing processes and cost structures.\(^7\)

Most of the patients reporting to the hospital for cancer treatment is from a low to medium socio economic class and find it difficult to pay the huge amount that is required to spend for the treatment. Manipal Hospital has its specialty centre for cancer treatment and research, which is sponsored by Shamdasani foundation, Mumbai. The medical social work wing under the department of
radiation oncology facilitates the patients from poor socio economic background to avail, such facilities for radiation therapy and other treatment related costs.

5.2.5 Clinical Outcome and the predictors of survival
Disease free or symptom free survival is one of the anticipated outcome measures of breast cancer treatment. In the present study the survival of breast cancer patients was estimated by Kaplan Meier survival analysis, considering symptom free survival as the event of interest for all the 3 treatment regimens. The survival curve was quite longer in case of regimen I (mean survival 11.01 years). This is mainly because the treatment had been started in early stage of the disease. The mean survivals were 2.52 years and 1.10 years for regimen II and regimen III respectively. The Kaplan Meier survival curves of group II and group III revealed that both the groups have shorter duration of symptom free survival. This may be because in both cases the treatment has started after advancement of the disease. Cox proportional hazards model regression analysis, keeping survival as dependent variable and demographics, treatment variables and disease characteristics as co-variants, showed significant association between survival and adherence to treatment as well as stage of cancer at the time of diagnosis in predicting survival (HR=6.77, 95% CI= 3.15-14.55, p=<0.001, and HR=0.10, 95% CI=0.05-0.22, P=<0.001 respectively for adherence and stage). All other covariates such as age, disease grade, ER/PR status, and nodal metastasis, duration of illness and presence or absence of comorbidity were not significant in predicting the survival of breast cancer patients studied. However, there were statistically significant negative correlations between survival and age, organ metastasis at the time of diagnosis, duration of symptoms, and whether radiation treatment received or not, P=<0.05).

According to a report prepared by Globocan 2008, on cancer statistics, cancer survival tends to be poorer in developing countries, most likely because of a combination of a later stage at diagnosis and limited access to timely and standard treatment.
5.2.6. Predictor of adherence to treatment

The adherence to treatment is an important indicator to predict outcomes in disease management. This is very much true in case of cancer treatment. In the present study 88% were adherent to the treatment as per the suggestions of the healthcare providers and 12% were not adherent to the treatment and this had a negative impact on the survival of these patients. Even though the treatment options were expensive, family income was not identified as a significant predictor to adherence to treatment. The logistic regression analysis with adherence as dependant variable and different demographic, treatment and disease variables as independent variables, spouses support and distant /organ metastasis at the time of diagnosis was found as significant predictors in adherence to treatment (OR= 15.29,95% CI= .98-237.97,P=0.05,OR=37.47, 95%CI=1.06-1320.61, P=0.04, OR= 0.06, 95%CI=0.00 -0.99, P=0.04 for spouses support Vs other, widowed Vs other and distant metastasis at the time of diagnosis respectively), where as all other variables gave insignificant P values. Age of the patient at the time diagnosis was also found as a predictor to some extent, even though the P value is not within the 0.05 level of significance (P=0.08).

In the present study, 14.9% of the group had distant metastasis at the time of diagnosis. The psychological stress and physical difficulties experienced by the advanced disease stage along with the unwanted effects of the therapies may make the patient refraining from certain aggressive treatment procedures during follow ups, which may put the patient in trouble and confusion, may miss necessary further steps and become non adherent to treatment. This will certainly have a negative impact on prolonged disease free survival. In certain cases there may be relief from symptoms, which may mislead the patient or patient party that the disease has been cured and avoid the aggressive treatment procedures, making the prognosis poor. Thorough counseling regarding the disease, treatment factors and the need to be adherent to the treatment is to be planned at the onset of treatment for patients as well as the care givers from the
family. This will certainly improve the adherence to treatment and survival. Pharmaceutical care programs, as suggested by the World Health Organization (WHO) is a suitable model for continuous care where in pharmacists can play a relevant role in improving health of the patients reducing cancer burden.\textsuperscript{79}

5.2.7. Patient reported humanistic outcomes

The patient reported humanistic outcomes after breast cancer treatment was documented for 226 patients, who were treated with drug regimens I, II and III. The quality of life measured in different domains of functional scores and symptom scores, revealed that there were differences in quality of life among patients under different drug regimens. Different domains of functions studied by EORTC QLQ C 30 and QLQ BR 23 were physical, role, emotional, cognitive, and social functions, including body image, future perspectives and global health. Except social functioning and future perspective, all functional scores were \( \geq 60 \) in patients under regimen III (ACT regimen). Those patients belonging to regimens II (FAC regimen) had low scores of functions in different domains and in the overall quality of life, when compared with regimen I (AC regimen) and regimen III. The symptoms experienced after chemotherapy was least for regimen III patients, when compared with the patients under regimen II and I. The over all quality of life of the subjects studied was best in regimens III patients. Comparison of means by one way ANOVA amongst the 3 drug regimens revealed that there were significant differences in the quality of life in Physical, role, and emotional functions and in global health (P value\textless{} 0.05).

Multiple comparisons test by Post hoc analysis (Tukey test) revealed that there are differences within the groups in physical, role, emotional and global health quality of life scores between the groups of FAC (regimen II) versus AC+Taxol (regimen III,\( D=0.001, 0.001, 0.048 \)and 0.009 respectively).

Dubashi et al conducted a study to find the quality of life issues using EORTC QLQ C 30 and BR 23 questionnaire among young women in an Indian tertiary
care hospital and found that the mean global health of the group was 77.93%. The functional scores of young breast cancer patients had better values, as high as 80-89%. The symptom scores also were as low as 5-20% except in financial score of the symptoms. The result of present study was not matching with the study findings of above mentioned authors. In the present study, different functional scales were found in the range 50-70% in physical, role, emotional and cognitive functioning. Future perspectives and social functioning scores were less than 50 % in patients under all the three regimens. Upset by hair loss and financial constrains were the maximum scored symptoms in all the three groups (70-82%). Systemic therapy side effects ranged from 43- 47% in all 3 categories.

Debess et al conducted a study to assess cognitive function, quality of life and psychological distress after surgery for early breast cancer in Denmark and found that breast cancer patients had a significantly 3-4 fold increased risk of experiencing cognitive impairment, when compared to the controls. Quality of life and psychological distress were also significantly poor among patients. The present study also found that there is reduction in quality of life in general and in cognitive function and is agreement with the above report.

Dhanya et al conducted a study to compare the toxicity experience (WHO toxicity grade) after chemotherapy in two groups FAC versus ACT among the breast cancer patients at regional cancer centre Trivandrum and found that there was significant increase in toxicities such as anemia, hyper pigmentation, stomatitis, and diarrhea in the FAC regimen group, while leukopenia, myalgia, arthralgia and peripheral neuropathy were more common, with the ACT regimen. Comparison of the two regimens revealed that all patients on the ACT regimen developed leukopenia, whereas, only 33% of the FAC developed leukopenia. Nausea and vomiting was reported as most intolerable among these patients. The authors reported that these two regimens had different toxicity profiles.
The present study carried out for comparing the humanistic outcomes after three commonly used chemotherapy regimens found that unwanted effects in different forms and degrees were very common with cytotoxic drugs. Fatigue, systemic therapy side effects, diarrhea and sleep loss was maximum in FAC regimen, and least in ACT regimen. Even though there are slight differences in the symptoms scores among the 3, one way ANOVA revealed statistically insignificant P values except for constipation and upset by hair loss (P=0.03 and 0.022 respectively). Post hoc analysis for multiple comparisons by Tukey test showed that there differences between the groups except with respect to pain, constipation and hair loss (D=0.154, 0.048 and 0.98 respectively).

5.3. Conclusions

In India, the number of cancer cases at present is placed at approximately 15 lakhs. This number is rising by 7 to 8 lakhs each year and if not checked may cross the 1 million very soon. The reasons for this phenomenal increase in the incidence of cancer in India can be attributed to a number of factors of which the most important undoubtedly are the increase in the life span of an average Indian from 52 years to 63 years, the hold of the tobacco habit, our changing lifestyles and the degradation of our environment.

The breast cancer care is an important issue in public health of women today. The burden of breast cancer has impact not only on the patient, but also on the family, community and the nation at large. Quality care can improve the quality of life and survival of the affected and reduce the morbidity, bringing relief to all above. Recent studies in India have shown that infiltrating ductal carcinoma is the most commonly diagnosed histopathology type of breast cancer. The mean age of onset and diagnosis for breast cancer is a decade earlier in Indian patients, when compared to western women.

Due to discrepancies like ignorance, poor socioeconomic status, fear of suffering due to disease and treatment, the patients refrain from reporting to the
hospital for diagnosis and treatment. The screening options like mammography and histopathology tests are not available to a larger population; if available it is very expensive. This drawback makes the patient to postpone the screening for breast cancer and diagnosis at an early stage. Many women are reporting the disease in advanced stage of breast cancer. This makes treatment difficult and expensive bringing poor outcomes.

In order to have access to screening for early detection of cancer among Indian patients, we must develop some cost effective means. Awareness programmes and training for breast self examination can be a cost effective methods affordable to all socio economic classes. BSE should be promoted among the women in rural and urban areas. This will speed up the reporting, leading to biopsies and early detection.

Conventional treatment such as surgery, chemotherapy, radiotherapy and treatment with monoclonal antibodies are available in India. Usually combination of different treatments is preferred over a single treatment. The efficiency of treatment mainly depends upon the stage of cancer at the time of diagnosis, the adherence to treatment and patient specific factors. Many of our patients are not in a position to avail the facilities, mainly because of cost factor. It is very important that access to different treatment options be made available cost effectively for common people. It is advisable that governments and other charitable organizations or pharmaceutical companies, establish different insurance schemes especially for those who are below poverty line and cannot afford cancer treatment.

What is required is to make the public aware of the facilities available in the country (Refer. Appendix pages - Contributions of Indian Cancer Society and other NGOs for cancer prevention and treatment). For this the co operation and co ordination of activities of health care sector are to be strengthened. Awareness programmes on different cancers and their relationship with the lifestyle and diets will be beneficial in cancer prevention. Many cancers can be prevented by lifestyle modifications such as cessation of tobacco use, avoiding
alcoholic drinks, engaging in regular exercise and such other activities. Above all women must be advised to have a watch on, for any early warning signs of breast cancer.

5.4. Implications

The findings of the study have thrown light on existing conditions and treatment approaches for breast cancer in a tertiary care teaching hospital. The study results have implications for the current and future healthcare delivery.

Caring women with breast cancer is a challenge to the healthcare provider. Interventions in cancer care are focused not only on ensuring or prolonging survival, but also on improving the quality of life of those who are surviving. This study clearly updates the situation of economic, clinical and humanistic outcomes of breast cancer patients. The cost of conventional therapies is expensive and beyond the reach of middle and lower categories of socio economic background. In fact different facilities are available for cost effective cancer treatment in the country. Many often this is underutilized by the deserving candidates, mainly due to ignorance. This could be popularized among the public by campaigns and other suitable means. The information obtained by the present study will be a baseline for planning such activities in the health care sector.

Inclusion of quality of life assessment in practice is a valuable message to patients that we care about the person with cancer and QOL is the ultimate goal of oncology practice. QOL assessment offers a patient-centered approach to study the various factors that affect patient centered outcomes of the individual or population. Assessing QOL can provide new insight into the health care experience and is capable of improving healthcare delivery. The findings of the study help to broaden the understanding of various psychosocial aspects faced by the breast cancer patient in India and provide progressive recommendations to improve the QOL of patients suffering from breast cancer.
Basic education of pharmacists is to be framed incorporating patient centered pharmacy practice and preparing pharmacists to meet the needs of patients diagnosed with cancer. The need for a curriculum change in the oncology pharmacy practice speciality may be considered for preparing qualified pharmacy professionals to provide patient centered care and improve quality of life of cancer patients. Oncology pharmacy practice can lead to many revolutions in cancer patient care and research is the basis for all such revolutions. Cancer clinical trials with quality of life tools and other instruments have provided solid evidences for decision makers and stakeholders. Such research will bring better picture on the effectiveness of the treatment. The finding of this study can form a base for larger randomized controlled trials on breast cancer patients in different settings.

5.5. Limitations

The following limitations are felt at the end of this study.

1. The subjects included in this study were from one tertiary care hospital from private sector and hence generalization of the results is difficult.
2. Patients reporting to this hospital mostly belong to Karnataka and some parts of Kerala, in the vicinity of Manipal. Hence patient behavior described may be limited to the breast cancer patients from Karnataka and Kerala states.
3. The study setting was fixed to one center, which limits the generalization of results.
4. Due to the elaborate instrument, some of the subjects were impatient to complete the questionnaire. This reduced the effective sample size.
5. All the patients enrolled in the study could not be considered for complete echo model evaluations.
6. The sample size was inadequate for outcome measures due to incomplete data of some patients making generalization of the results difficult on global scales.
7. The indirect cost of treatment could not be estimated, which make the economic evaluation incomplete.

5.6. Recommendations

In the light of the findings, it can be recommended that

1. An evaluative study may be conducted to investigate the effectiveness of any interventions on improving the quality of life of breast cancer patients.
2. A prospective study may be conducted to find the quality of life during different points of treatment of breast cancer patients.
3. A systematic pharmacoeconomic evaluation may be carried out among different options in the management of chemotherapy induced nausea and vomiting.
4. An evaluative study may be carried out to find out the added advantage of herceptin therapy in breast cancer management with more number of subjects.