World Academy of Science, Engineering and Technology
International Journal of Medical and Health Sciences
Vol:9, No:1, 2015

Assessing Chemo-Radiotherapy Induced Toxicity and Quality of Life of Cancer Patients

A. Taqaddas

***Abstract*—**Chemotherapy and radiotherapy are one of the major treatment modalities that play important role in the management of a number of different cancers. This study for the first time evaluates the toxicity of these treatment modalities and its impact on quality of life of cancer patients in Pakistan. The study also for the first time determines what cancer patients of different ages and cancer stages believe would be an effective intervention to manage their psychosocial needs and treatment induced toxicity. The article also provides evidence based approach for the use of variety of interventions to mange cancer treatment induced morbidity and toxicity. In light of the present study and reviewed research data, evidence based recommendations are also made for selection of appropriate interventions to manage Pain, Nausea and Vomiting, Anxiety and Depression, Fatigue and Overall QOL of cancer survivors.

***Keywords*—**Chemotherapy Toxicity, Psycho-Social Interventions, Quality of Life, Radiotherapy Toxicity.

I. Introduction

IN 2012, 14.1 million new cases of cancers were diagnosed worldwide and 8.2 million cancer deaths were reported [1]. Chemotherapy, surgery and Radiotherapy usually act as standard of care for most cancer patients. Chemotherapy and radiotherapy can give rise to acute and long term side effects that in turn can significantly compromise patient's quality of life. Hence identification of overall chemotherapy and Radiotherapy toxicity profile (acute and long term) can help refine application of Chemotherapy and RT in terms of better scheduling treatment for cancer patients and in identifying Patients preferences and risks of developing certain toxicities. There is notable gaps in the literature regarding the cancer treatment specific psychosocial issues, treatment induced toxicities and availability of psychosocial interventions for cancer patients in Pakistan. This study highlights various toxicities experienced by cancer patients in Pakistan discussing their magnitude, their impact on patient's quality of life and their possible management strategies. Hence this study is aimed at bridging this gap by finding out what treatment toxicities cancer patients in Pakistan experience, how disease and its treatment impacts their QOL and what psychosocial interventions they feel can improve their QOL. Recommendations to manage different treatment induced toxicities by using interventions will also be presented. According to World Health Organization (WHO) the most common causes of cancer mortality in 2012 were lung, liver, and stomach cancers and the most prevalent newly diagnosed cases are lung, breast, and colorectal cancers [1]. Most studies in the literature discuss breast cancer and prostate cancer specific toxicities in detail and thus there is shortage of studies that discuss other cancers. Therefore the researcher of the present study has selected a combination of most commonly occurring cancers along with a less prevalent cancer i.e. Breast, Lung, colon and osteosarcoma. Glossary is provided at the end in the Appendix D.

No financial support was involved in carrying out this research project.

A. Taqaddas is with Research Wormhole and JMIRS, Canada (e-mail: taqaddas@mail.com).

II. Materials and Method

A. Study Overview

Six cancer patients with a variety of malignancies were included in this study. The survey was conducted between the periods of 1st Nov – 10th Nov 2014. Chemotherapy and radiotherapy induced toxicities and the quality of life of cancer patients was assessed using a self reported survey comprising 28 items. See Appendix A. The present study used researcher designed questionnaire. The questionnaire was designed in the light of brief literature review. The questionnaire was supplied with invitation letter and one page supplementary information to help cancer patients understand purpose of the study, difficult terms and to make it slightly easy for them to fill it in.

The scores of items ranged from 0 to 10 on QOL questions, coping item, functional scales, treatment induced side effect of most concern and financial difficulties items. Symptom scale included 21 items that are each scored on a scale from 0 (None or no change) to 4 (Complete loss of function) i.e. Common toxicity Criteria version 2 was used for toxicity grading [2]. Higher scores denote better QOL for functional scales whereas higher scores on symptom scales and items denote worse health for symptom scales and items. Late effects were defined as toxicity apparent after 3 months.

The `primary outcome measure for the study was determination of most commonly reported chemotherapy and radiation induced acute toxicities in cancer patients treated in Pakistan. Secondary outcomes include determination of QOL of cancer patients, identification of Chemotherapy and Radiotherapy treatment related side effects that are of most concern to cancer patients, late chemotherapy and Radiotherapy induced toxicities and presence or lack of various interventions to deal with psychosocial issues of cancer patients. All six cancer patients were treated at a single cancer centre in city of Lahore, Pakistan.

B. Eligibility Criteria

Eligible patients had confirmed diagnosis of Cancer, aged 18 years or more and agreed to participate in the study.

Questionnaires were delivered to six cancer patients who have either completed their cancer treatment or are undergoing cancer therapy. Some of the cancer patients were acquaintances of the researcher who agreed to participate in the study and then these patients then asked other cancer patients to participate in the survey.

C. Ethical Approval

No patient records or hospital treatment records including scans were accessed. No personal data was collected through the survey. Hence no ethical approval was required. Patients were informed that this survey is being conducted for research purposes. Patients were also informed that the data derived from this survey will be used to try to find out ways to improve patients QOL and management of treatment induced toxicity. All these cancer patients from a single cancer centre willingly agreed to participate in the present study.

D. Statistical Analysis

Descriptive statistics (mean, median, mode, Range and percentages) were used to describe data.

III. Results

The results for each question in the survey are described below in the order that makes reading and understanding this article easy. For example results for chemotherapy induced and RT induced acute and long term toxicity are described close to one another. For most patients key scores were calculated by removing those who did not answer at all or who said they don't know or can't remember. In case of question 14 (Radiation and chemotherapy induced Acute toxicity) three patients were not considered when determining RT induced acute toxicity. Colon cancer patient did not answer the question at all, the ca lung patient did not answer radiation induced side effects part of question 14 and advanced breast cancer patient partly answered question 14 and failed to grade any toxicity. Results are shown in Figs. 1-16 and in Tables I-XIV. Appendix B and C contain explanation for results of number of chemotherapy cycles and results for Chemotherapy Induced Acute Toxicity respectively.

A. Positive Findings of the Survey

Some of the positive findings of this survey are listed below:

Q23. Patients being told how to manage or control side effects: 83.3% patients were explained clearly by health care staff how to manage their side effects.

Q24. Staff did everything possible to control the side effects: 100% of patients said they did.

Q26. Patients rating of overall health care support they received during and after treatment: 66.6% of patients reported Excellent or very good care. 99.9% of patients rated good and greater than good.

Q27. Psychosocial support offered to patients: 66.7% (i.e. 4) patients said they were offered psychosocial interventions to deal with psychosocial aspects of treatment and its side effects.

Q14. Chemotherapy and RT induced acute toxicities and their magnitude (grade): No grade 4 toxicity was observed i.e. 0%.

B. Response Rate

Response rate was 100% i.e. all 6 patients filled in and returned the survey. This indicates willingness of cancer patients to describe their experience in terms of their treatment and side effects. High response rates (70%) were also reported by RT Patient Experience Survey 2013 conducted in England [3].

C. Patient Demographic and Clinical Information

The survey included some questions asking for demographic, disease and treatment related information and the results are shown in Tables I-IV. The result tables show number of respondents and percentages by gender, age, occupation, Long Term Condition (LTC), Type of Cancer, Stage of disease, Treatment intent, presence/absence of concurrent Chemo-RT.

Median age at the time of diagnosis in the study was between 50-60 Years. There were 3 males and 3 females. 5 patients (83.3%) were married and one (16.7%) was single. Three (50%) patients suffered from breast cancer and one (16.7%) patient had lung cancer, one (16.7%) colon cancer and one (16.7%) osteosarcoma. Most patients had early stage I-II (66.7%) disease whereas the rest (33.3%) had stage III-IV advance disease. Four patients received chemotherapy and Radiotherapy concurrently. 83.3% (5) of patients received treatment with curative intent and 16.7% (1) with palliative intent. All 6 patients (100%) received chemotherapy, 4 patients received radiotherapy as well as chemotherapy. The results for surgery had to be corrected. One breast patient did not indicate surgery and one Osteosarcoma patient had amputation of one leg but did not select surgery as one of the treatments for cancer. After correction it seems that in total 5 patients had surgery.

TABLE I
Patient Characteristics

Cases	Cancer	S	TA	Gen	Age(Years)	MS	Occ
BR1	Breast	E	C	F	40-50	M	HW
BR2	Breast	E	C	F	40-50	M	HW
BR3	Breast	A	C	F	50-60	M	HW
LG4	Lung	E	C	M	30-40	M	ITP
CN5	Colon	A	P	M	40-50	M	Bshop
OS6	Osteosar	E	C	M	< 30	S	St

Note: Osteosar=osteosarcoma, S= stage, E=Early, A=Advance, Gen= Gender, TA= Treatment Aim, Occ=Occupation, HW= House Wife, ITP= IT Professional, B-shop=Business-Auto Shop, St=Student, F=Female, M= Male, MS= Marital Status.

D. Long Term Conditions (LTC)

Patients were asked if they suffer from any Long Term Conditions. The results are shown in Table IV.

66.7% of patients said they suffer from no Long term condition. Only one patient (16.7%) said she suffers from Diabetes but she did not have diabetes at the time of cancer diagnosis.

TABLE II
DEMOGRAPHIC RESULTS

Demographic Categories	No of respondents	Percentage
Gender		
Male	3	50%
Female	3	50%
Age		
Less than 30 Years	1	16.7%
30-40 Years	1	16.7%
40-50 Years	3	50%
50-60 Years	1	16.6%
Above 70 Years	0	0%
Mean Age	46.6 Years	
Median Age	50 Years	
Marital Status		
Single	1	16.7%
Married	5	83.3%
Divorced	0	0%
Separated	0	0%
Occupation		
House Wife	3	50%
IT Professional	1	16.7%
Business: Auto Shop	1	16.7%
Student	1	16.7%

TABLE III
RESULTS FOR CLINICAL CHARACTERISTICS

Clinical Characteristics	No of respondents	Percentage
Cancer		
Breast Cancer	3	50%
Lung Cancer	1	16.7%
Colon Cancer	1	16.7%
Osteosarcoma	1	16.7%
Cancer Stage		
Early stage I-II	4	66.7%
Advanced Stage III-IV	2	33.3%
Treatment Aim		
Cure	5	83.3%
Palliation	1	16.7%
Don't Know/Can't Remember	0	0%
Missing Information	0	0%
Concurrent Chemo and RT treatment		
Yes	2	33.33%
No	4	66.7%

TABLE IV
LONG TERM CONDITIONS

LTC	No of Respondents	Percentage
Blindness	0	0%
Deafness	0	0%
Mental Health Condition	0	0%
Learning Disability	0	0%
Long standing illness	1	16.7%
No LTC	4	66.7%
Missing Information	1	16.7%

E. Duration of Chemotherapy Course

The data filled in by cancer patients for chemotherapy cycles was not very clear. Hence logical assumptions have been made to derive some sense out of it. See Appendix B for explanation.

Patients had a median number of chemotherapy cycles of 4 and range was 7 (1-8 cycles).

TABLE V
CHEMOTHERAPY COURSE DURATION

Patients	Cycles	Weeks	Gap
BR1	4 cycles	-	3 weeks
BR2	6 cycles	**18 weeks**	3 week (1 cycle followed by 3 week Gap)
BR3	**1 cycle**	3weeks	-
LG4	**4 cycles**	12 weeks (3months)	-
CN5	8 Cycles	-	3 weeks
OS6	**1 cycle (every 35 days)**	-	5 weeks
Missing Information	3 patients (BR3,LG4,6OS)	-	
Median CT Cycles	4		
Range	7		

Note: Results shown in bold are assumptions made from the survey results for the purposes of analysis where patient supplied information was either not clear or was insufficient. CT=Chemotherapy

F. Chemotherapy and RT-Induced Long Term Toxicity

Weight loss was the most prevalent chemotherapy induced late side effects mentioned by 33.3% of respondents. These respondents had cancer of lung and colon. Weakness, Fatigue and Tiredness and weak eye sight were among other chemotherapy induced side effects mentioned by other cancer patients. Among RT induced late side effects 16.7% of patients mentioned Fatigue and tiredness and another 16.7% of respondents cited Weak eye sight as a late RT induced side effect. One patient did not mention any late side effects. Results are shown in Table VI and Fig. 1.

TABLE VI
CHEMOTHERAPY-RT LATE TOXICITY

Late Toxicity	No of Respondents	Percentage
Chemotherapy	5	83.3%
RT	2	33.3%
Missing CT Info	1	16.7%
Missing RT Info	3	66.7%
Don't Know/Can't remember (RT)	1	16.7%
Don't Know/Can't Remember (CT)	0	0%

Note: CT=Chemotherapy, RT=Radiotherapy

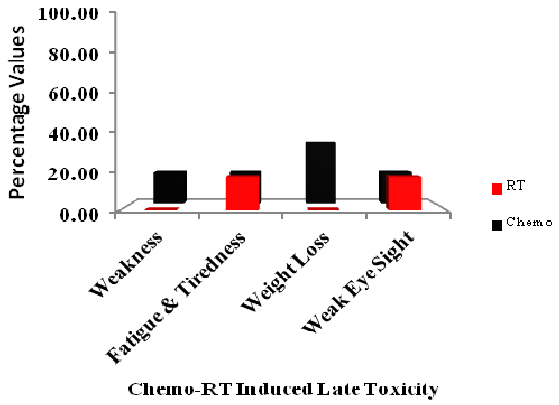


Fig. 1 Chemo-RT Induced Late Toxicity Profile

G. Chemotherapy Induced Acute Toxicity

Figs. 2-16 and Tables X–XIV (Appendix C) show the results for Chemotherapy Induced Acute Toxicity. Overall no grade 4 toxicity was observed. The worst rated symptoms

were Hair loss (total score=12), Anxiety and Depression (total score=11), Pain (total score=10), Tiredness and Fatigue (Total score=8) and Nausea and Vomiting (Total score= 7). The most common chemotherapy induced toxicity was G2/3 Hair loss (66.7%), Anxiety and Depression (66.7%), Pain (66.7%) followed by Tiredness and Fatigue (50%) and Nausea and Vomiting, NV (50%).

Hair loss, anxiety and depression, and tiredness and fatigue have received a median and mode ratings of 3 where as Pain had a median 2.5 and a bimodal rating of 2,3 and Nausea and vomiting received a median and mode rating of 2 on a scale of 0 (none) to 4 (complete loss of function) and high percentage (66.6% and 50% respectively).

Overall majority of breast cancer patients reported severe (G2/3) Hair loss (66.7%), anxiety and Depression (66.7%), Pain (66.7%), Tiredness and Fatigue (66.7%) and Peripheral neuropathy (66.7%), Appetite loss (66.7%) followed by constipation (33.3%), Esophagitis (33.3%), Skin changes, Insomnia, Drowsiness and Other (33.3%) symptoms. NV was reported by 66.7% of breast cancer patients out of which 33.3% reported G2 NV. Note Hair loss and Anxiety and Depression were reported by all three breast cancer patients (100%). One breast cancer patient out of 3 reported severe insomnia (i.e. grade 3) another one did not answer at all and the third one reported no insomnia (i.e. Grade 0). However insomnia can be one of the major side effects for breast cancer patients undergoing chemotherapy but due to small number of participants in this study this trend was not obvious.

Overall Lung cancer patient reported G2/3 Hair loss, Anxiety and Depression, Pain, Tiredness and Fatigue, NV, Diarrhoea, Mouth Ulcer/soreness, Appetite loss and Skin changes. G1 Insomnia, Peripheral neuropathy and other symptoms were reported by lung cancer patient.

Overall Osteosarcoma patients reported G2/3 Hair loss, Anxiety and Depression, Pain, NV, Shortness of breath, Dyspnoea, Insomnia, Tissue Fibrosis, Drowsiness and other symptoms and G1 Bowel problems, Dry cough and skin changes. BR3 patient either did not answer listed toxicities or did not grade them. Ca colon patient did not report any chemotherapy and RT induced toxicity.

1. Dermatological Toxicity

16.7% did not report any skin changes i.e. they had Grade 0 toxicity. 33.3% reported Grade 2 toxicity. No grade 3 and 4 toxicity was reported where as 33.3% of patients did not answer at all. 83.3% of patients reported alopecia out of which 16.7% did not grade the toxicity. 66.6% of patients developed severe alopecia (G2/3).

2. Upper Gastro-Intestinal Tract (GI) Toxicity

Grade 2/3 Esophagitis was seen in 16.7% of patients (BR2) whereas 33.3% did not report any Esophagitis (Grade 0). Grade 2 mouth ulcer was reported by lung cancer patient (167%). 33.3% of patients did not report any mouth ulcer or soreness. G2/3 Appetite loss was seen in 50% of patients i.e. in breast cancer (BR1, BR2) and lung cancer patients. 83.3% of patients reported chemotherapy induced NV out of which one patient (167%) did not grade the toxicity. G2/3 NV was seen in 50% of patients where as 16.7% of patients did not report any NV.

The Osteosarcoma patient reported G2 shortness of breath accounting for 16.7% of G2/3 toxicity. 50% of patients did not report any shortness of breath. 16.7% of patients reported dyspnoea (again it was OS6 patient) and 50% did not report any dyspnoea.

Dry cough was reported by 83.3% of patients out of which 1.7% did not grade the toxicity. G0/1 dry cough was reported by 66.7% of patients. No G2/3 toxicity was reported by anyone.

In general patients receiving chemotherapy reported chemotherapy induced nausea and vomiting. In the present study no trend or association was observed between number of chemotherapy cycles and severe acute Nausea and vomiting. This was partly due to small number of participants and also due to insufficient information supplied by respondents to this survey.

2.1. Prevalence Rates for NV

Prevalence rates for Nausea and vomiting were 83.3%. Severe emesis was reported by 50 % of cancer patients (G2/3). Occurrence of severe Nausea and vomiting was low for breast cancer patients i.e. only 2 out of 3 breast patients reported nausea and vomiting. Out of these two only one patient reported grade 2 nausea and vomiting (16.7%) and another patient reported NV but did not grade it (PN). The third breast cancer patient did not report any nausea and vomiting (i.e. she reported Grade=0 NV). No patient reported grade 4 nausea and vomiting (0%). Low prevalence of severe (Grade 4) Nausea and vomiting in breast cancer patients was also observed by [4]. Booth and colleagues [4] argued early stage disease as one of the factors for experiencing low emesis. This could well be the reason for low prevalence of emesis in breast cancer patients in our study. Two out of three breast cancer patients had early stage disease and therefore probably had better performance status making them less prone to severe emesis. Overall 66.7% of cancer patients in the present study had early stage disease which could have resulted in 0% grade 4 symptoms.

2.2. Use of Anti-Emetics to Control NV

One breast cancer patient who received 4 cycles of chemotherapy said her Nausea and vomiting was controlled by medication. This could mean that modern antiemetics are able to reduce the severity and prevalence of chemotherapy induced emesis.

2.3. Risk Factors for Severe NV

In the present study patient OS6 having osteosarcoma with age less than 30 years reported grade 3 nausea and vomiting. Therefore Younger age may be a risk factor for severe Nausea and vomiting. Booth and Colleagues [4] also identified younger age as a risk factor for chemotherapy induced NV. Other reasons for experiencing severed NV may be due to different chemotherapy regimen. Operable Osteosarcoma patients usually receive chemotherapy regimen carrying very

high (Cisplatin – greater than 90% frequency without antiemetics) to moderate (Doxorubicin and Methotrexate – 30-90% frequency without antiemetics) emetogenetic potential chemotherapy drugs [5]. This patient also received chemotherapy and Radiotherapy concurrently. This could have been an added risk factor for severe emesis. One advanced stage breast cancer patient also received concurrent Chemo-RT and she also consequently experienced NV but she did not grade it. Hence Concurrent Chemo-RT may be a risk factor for severe NV but due to small number of cases in this study it is difficult to make a definitive conclusion.

3. Neurological Toxicity

Peripheral neuropathy was observed in 50% of patients. G2/3 peripheral neuropathy was seen in 33.3% where as G0/1 peripheral neuropathy was seen in 16.7%. Peripheral neuropathy was common in breast cancer patients as two out of three breast cancer patients reported the toxicity. One lung cancer patient also reported Grade 1 peripheral neuropathy. Bhal and colleagues [6] also reported chemotherapy induced sensory neuropathy in 38% of lung cancer patients. However they reported higher G1 toxicity (33.3%) than G2 toxicity (5%) after 3 rd cycle of chemotherapy. The symptoms of Hair loss, peripheral neuropathy and NV were found to get worse and had higher scores during chemotherapy treatment of mesothelioma lung patients [7]. The findings of the study by Nowak and colleagues 2004 are partly in agreement with the findings of the present study. In the present study lung cancer patients reported G1 peripheral neuropathy and G2 NV.

4. Pain

Pain was reported by Breast cancer (BR1, BR2), Osteosarcoma and lung cancer patients. 66.6% reported G2/3 pain while 0% had G0/1 toxicity.

5. Drowsiness

33.3% of patients did not report any drowsiness and 33.3% reported grade 2 drowsiness (i.e. BR2 and OS6). No grade 3 and 4 drowsiness was reported.

6. Anxiety and Depression

Overall Anxiety and Depression, Tiredness and Fatigue and Pain seemed to be directly related to Insomnia. Anxiety and Depression was reported by 83.3% of patients out of which 16.7% did not grade the toxicity (PN). High grade (Grade 3) anxiety and Depression was seen in Breast cancer (BR1, BR2) and osteosarcoma patients. In literature the prevalence of depressive symptoms ranges from 10-25% whereas Anxiety symptoms range from 10-30% [8, 9].

6.1. Trends between High rates of Anxiety and Depression and High rates of NV

There is also some indication that higher rates of anxiety and depression (83.3%) and more severe symptoms (G2/3 = 66.7% with most commonly occurring anxiety toxicity grade being 3) may contribute to higher rates of nausea and vomiting (83.3%) and more severe nausea and vomiting (G2/3= 50% with most commonly occurring nausea and vomiting toxicity grade 2) symptoms. At least 50% of patients reported grade <=3 anxiety and depression symptoms (median = 3). Overall a positive trend exists between more severe anxiety and depression and more severe NV.

7. Tiredness and Fatigue

Tiredness and Fatigue was seen in 50% of patients and was the 4th worst rated toxicity with all patients reporting G2/3 toxicity and none of the patients reported G0/1 toxicity. Breast cancer (BR1, BR2) and Lung cancer (LG3) patients reported G2/3 Tiredness and Fatigue. Studies have reported cancer related fatigue in the range of 60-90% [10]. Bhal and colleagues [6] reported G2 and G1 fatigue in 45.9% and 51.35% of lung cancer respectively. In the present study no G0/1 tiredness and fatigue has been reported. However the lung cancer patient reported severe tiredness and fatigue (Grade 3).

8. Insomnia

G2/3 Insomnia was seen in 33.3% of patients and 16.7 % had no sleep disturbances where as another 16.7% reported Grade 1 insomnia.

8.1. Trends between Severe Anxiety and Depression and Severe Insomnia

It has been observed that high frequency of anxiety and depression (83.3%) and severe anxiety and depression symptoms (G2/3=66.7%) seems to be related with more severe insomnia (G2/3= 33.3%) with most commonly occurring insomnia toxicity grade 3. Exception was Patient 2BR who reported grade 3 anxiety but did not report any insomnia.

8.2. Trends between Tiredness and Fatigue and Insomnia

Tiredness and fatigue can also contribute to insomnia. In the present study patient BR1, BR2, LG4 reported tiredness and fatigues and patient OS6 reported general weakness. All these patients also reported insomnia except patient BR2. Patient BR2 did not suffer insomnia and it could be due to strong family support and use of healthy diet that counterbalanced the effects of tiredness and fatigue on insomnia.

8.3. Trends between Severe Pain and Severe Insomnia

Similarly high frequency of pain (66.7%) and more severe pain symptoms (G2/3= 66.7%) seems to result in more severe insomnia rates with at least 50% of patients reporting grade 1 and 3 insomnia (median = 2). Two patients reported G3 pain and they also suffered from G3 insomnia.

Overall patients with pain, anxiety and depression exhibited insomnia except in case of patient BR2. Patient BR2 had lot of family support and she also suffered less pain therefore it may be one of the reasons for not reporting or experiencing any insomnia.

9. Lower Gastro-Intestinal Tract (GI) Toxicity

The least rated symptoms were Urinary and Bowel problems with total scores 0 and 1 respectively with no G2/3 toxicities and 66.7% of G0/1 toxicities. 66.7% of patients did not report any Urinary problems (i.e. grade 0). 50% of patients

did not report any Bowel problems where as 16.7% reported Grade 1 bowel toxicity. No G2/3 urinary and bowel toxicity was reported by any patients.

Grade 2 constipation was reported by 16.7% of patients. It was patient BR1. 33.3% of patients did not report any constipation (i.e. they had Grade 0).

Lung cancer patient reported Grade 2 diarrhea. 33.3% of patients did not report any diarrhea.

10. Tissue Fibrosis

Grade 3 tissue fibrosis was reported by Osteosarcoma patient (16.7%). 50% of patients did not report any tissue fibrosis and 33.3% of patients did not answer at all.

11. Other Toxicities

Toxicities other than those listed were reported by Breast cancer (BR2), Osteosarcoma (OS6) and lung cancer patients (LG4). 33.3% of patients reported G2/3 other toxicity. The other toxicities reported by breast cancer patients included shoulder pain, and long term weakness. Lung cancer patient did not specify the toxicity but gave it a grade of 1. Osteosarcoma patient reported Grade 3 general weakness.

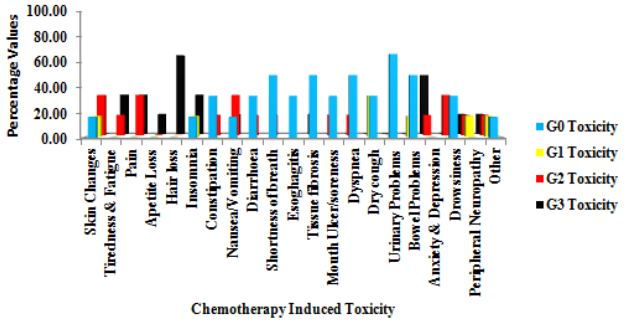


Fig. 2 Chemotherapy Induced Toxicity Profile

H.RT Induced Toxicity

Overall no grade 4 toxicity was observed. The worst rated RT induced toxicities were Tiredness and Fatigue and Pain with scores of 7 each followed by Peripheral neuropathy and skin changes with a total score of 5 and 4 respectively. G2/3 Tiredness and Fatigue and Pain were observed in 100% of patients making them the most common toxicities as well. The least rated toxicities were Appetite loss, Esophagitis, Mouth Ulcer/soreness, Dry Cough, Urinary Problems, Bowel Problem, Constipation and Diarrhoea. G0/1 Urinary Problems, Bowel Problem and dry cough and dyspnoea had highest percentages (100%).

No G2/3 Dry cough, Urinary problems and bowel problems were reported during Chemotherapy and RT. More grade 2/3 skin changes, tiredness and fatigue and pain occurred during RT compared to chemotherapy. More G2/3 Grade toxicities occurred during Chemotherapy and more G0/G1 toxicities occurred during RT.

I. QOL

QOL of patients during Radiotherapy (median=4, mode= 2, 4) was superior than QOL during chemotherapy (median=2.5, mode=2) whereas QOL in the past week (median=7.5, mode=8) was superior than both QOL during RT and chemotherapy.

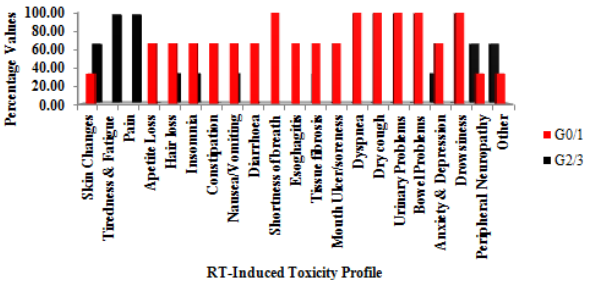


Fig. 3 RT-Induced Toxicity Profile

TABLE VII
ACUTE CHEMOTHERAPY AND RT TOXICITY DATA

	G0/G1 (Chemo)	G2/3 (Chemo)	G0/G1 (RT)	G2/3 (RT)
Acute Toxicity	**N = 6**		**N = 3**	
Skin Changes	2(33.3%)	2(33.3%)	1(33.3%)	2(66.7%)
Tiredness & Fatigue	0(0%)	3(50%)	0(0%)	3(100%)
Pain	0(0%)	4(66.7%)	0(0%)	3(100%)
Appetite Loss	0(0%)	3(50%)	2(66.7%)	0(0%)
Hair loss	0(0%)	4(66.6%)	2(66.7%)	1(33.3%)
Insomnia	2(33.3%)	2(33.3%)	2(66.7%)	1(33.3%)
Constipation	2(33.3%)	1(16.7%)	2(66.7%)	0(0%)
Nausea/Vomiting	1(16.7%)	3(50%)	2(66.7%)	1(33.3%)
Diarrhoea	2(33.3%)	1(16.7%)	2(66.7%)	0(0%)
Shortness of breath	3(50%)	1(16.7%)	3(100%)	0(0%)
Esoghagitis	2(33.3%)	1(16.7%)	2(66.7%)	0(0%)
Tissue fibrosis	3(50%)	1(16.7%)	2(66.7%)	1(33.3%)
Mouth Ulcer/soreness	2(33.3%)	1(16.7%)	2(66.7%)	0(0%)
Dyspnoea	3(50%)	1(16.7%)	3(100%)	0(0%)
Dry cough	4(66.7%)	0(0%)	3(100%)	0(0%)
Urinary Problems	4(66.7%)	0(0%)	3(100%)	0(0%)
Bowel Problems	4(66.7%)	0(0%)	3(100%)	0(0%)
Anxiety & Depression	0(0%)	4(66.6%)	2(66.7%)	1(33.3%)
Drowsiness	2(33.3%)	2(33.3%)	3(100%)	0(0%)
Peripheral Neuropathy	1(16.7%)	2(33.3%)	1(33.3%)	2(66.7%)
Other	2(33.3%)	2(33.3%)	1(33.3%)	2(66.7%)

Note: Number of patients reporting toxicity grade are shown outside the bracket

J. Coping Today As a Result of Treatment

50% patients gave a score of 5 (i.e. normal). 16.7% patients scored 7 and 33.3% scored below score 5.

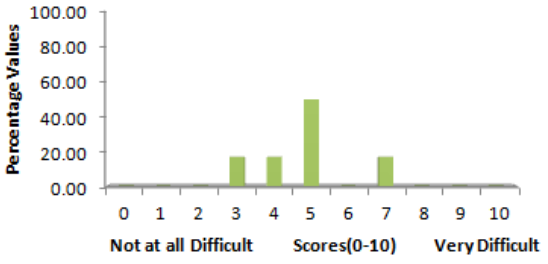


Fig. 4 Coping Today as a Result of Treatment

K. Problems with Family and Social Life and Managing in Home

Younger patients and patients with palliative treatment intent reported more difficulties with family, social and home life i.e. Osteosarcoma and Lung cancer patients.

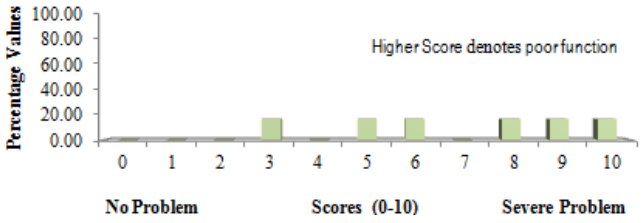


Fig. 5 Treatment & Disease Affect on Home Activities

66.6% of patients scored above 5 and 33.3% scored 5 and below on managing in Home.

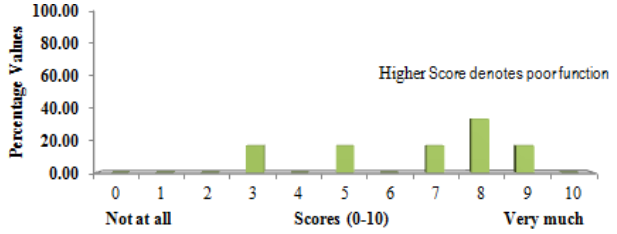


Fig. 6 Physical condition & Treatment Affect on Family & Social Life

66.6% of patients scored above 6 i.e. their family and social lives were very much affected by their physical condition and treatment whereas 33.3% scored 5 and below.

L. Financial Burden

33.3% of respondents experienced great financial difficulties.

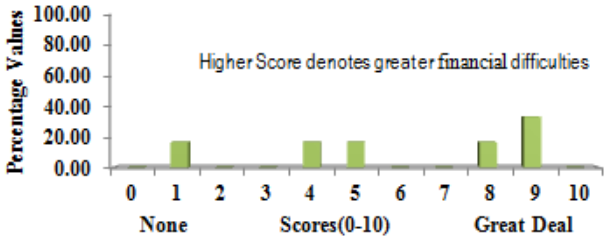


Fig. 7 Financial Burden due to Disease & Treatment

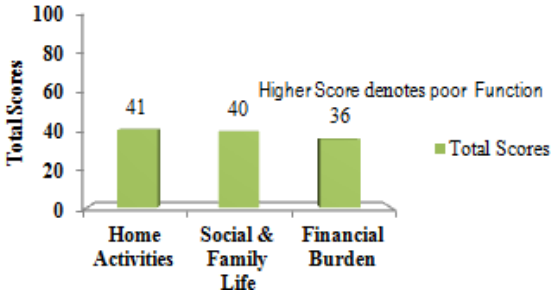


Fig. 8 Overall Scores for Home Activities, Social & Family Function & Financial burden

The overall scores for home activities, Social and Family life were 41 and 40 respectively out of a total score of 60. The overall score for financial burden was 36. Overall Home activities have the highest Total score and therefore were greatly affected by treatment and disease.

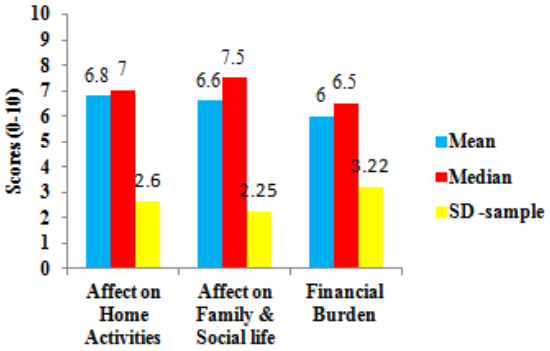


Fig. 9 Descriptive Statistics for Home Activities, Family & Social life and Financial Burden

Family and social life have the highest median i.e. 50% of the scores observed were <=7.5 followed by Home activities (median = 7).

M.Results for Treatment Induced Toxicities for Which Patients Were Most Concerned

Fatigue and Tiredness was the most prevalent treatment induced toxicity (33.3%) of most concern overall and among breast cancer patients. One breast cancer patient indicated concerns about 4 toxicities such as Muscular weakness, Tense nerves, Pain and Fatigue and Tiredness. The third breast cancer patient stated intracticable vomiting. Toxicity of most concern for Male cancer patients included infertility, skin discoloration, amputation and weak bone. For Osteosarcoma patient amputation and weak bone were treatment induced toxicities of most concern. For lung and colon cancer patients' infertility and skin discoloration were toxicities of highest concern respectively.

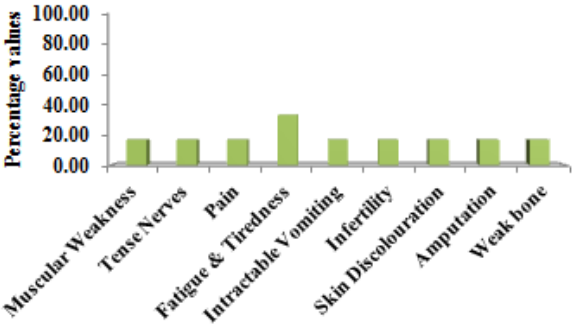


Fig. 10 Toxicities of Most Concern

N. Information on Managing Treatment Side Effects

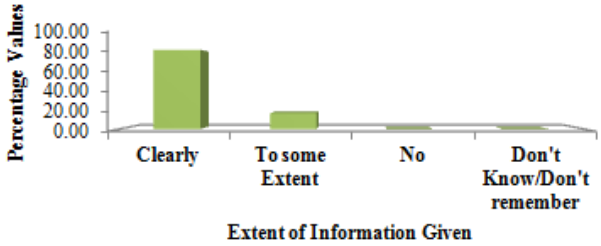


Fig. 11 Information Provided on Managing Treatment Side Effects

83.3% of patients said that clear information was provided by the hospital staff regarding managing treatment induced side effects and 16.7% of patients said they were provided with information to some extent.

O. Rating Staff Efforts to Manage Treatment Induced Side Effects

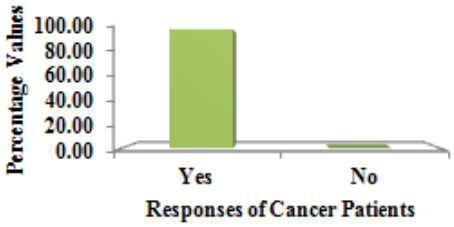


Fig. 12 Rating Staff Efforts in Managing Treatment Induced Side Effects

All patients (100%) said that the staff did everything possible to manage their treatment related side effects.

P. Rating For Health Care Support

33.3% of patients rated overall health care provided by the hospital excellent; another 33.3% rated the health service very good and another 33.3% good. Overall patient response was very positive.

Fig. 13 Overall Rating for Health Care Support

Q. Use of Medication to Manage Side Effects

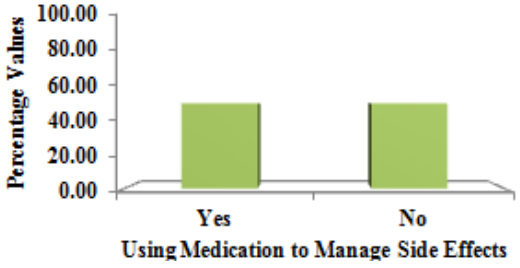


Fig. 14 Managing Side Effects with Use of Medication

50% of patients said that they use medication to control and manage their side effects where as remaining 50% do not use any medication. Among the two breast cancer patients who said they do not use medication currently were given medication when they were getting treatment. These patients have completed their treatment now and are not on any medication. Two patients mentioned the name of the medication they were using to manage treatment induced side effects. One was Ca breast patient and she was using Ondensteron and other was ca colon patient and was using chlorhexidine (BR3, CN5).

R. Interventions Offered to Patients to Manage Psycho-Social Issues

Patients were asked whether any interventions were offered to them to deal with the psychosocial aspects of their treatment and side effects. They were given some options to chose from or state other type of interventions that are not listed in the given options.

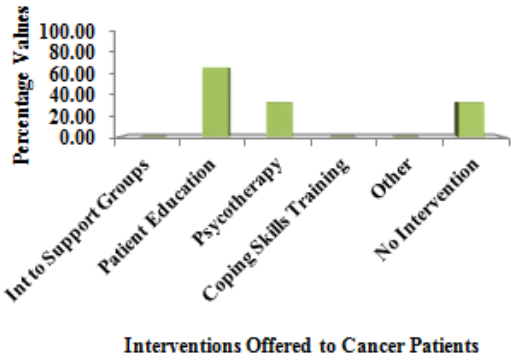


Fig. 15 Interventions Offered to Cancer Patients for Managing Treatment related Psycho-Social Issues

66.7% (4) patients were offered interventions to deal with psychosocial issues and 33.3% did not receive any intervention. The most prevalent mode of intervention was Patient education (66.7) followed by psychotherapy. Four patient received patient education out of which two patients received Patient education plus psychotherapy.

S. Improving QOL of Cancer Patients and Management of Treatment Related Side Effects

Patients were asked how their QOL and management of treatment side effects can be improved.

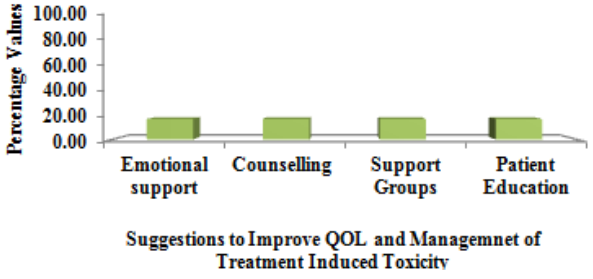


Fig. 16 Suggestions to Improve QOL and Management of Treatment Induced Toxicity

16.7% said treatment should be offered in a more polite, caring and sensitive manner referring towards emotional support, 16.7% said counselling should be offered with clear explanation of side effects, 16.7% said support groups and another 16.7% said patient education should be offered to patients to improve their QOL and management of treatment side effects.

IV. Analysis

A. Demographic Analysis

1. Gender

The Differences of view between men and women with respect to their QOL during RT and chemotherapy treatments were not very pronounced. However it was observed that male patients scored less positively in Chemotherapy QOL i.e. all 3 male patients scored below 5. With respect to QOL during RT both male and female respondents scores appeared almost same (i.e. two male and two female patients scored below 5) except that male patients did not score very encouragingly i.e. no scores above 5 were observed. On the other hand one female respondents scored positively on QOL during RT (score 8). The questions on which male respondents scored positively were QOL during past week. However this difference between male and female respondents was only nominal. The RT Patient experience survey conducted in England also found differences of opinions expressed by men and women with regards to their RT treatment [3].

2. Age

In the present study older age appeared to be linked with better QOL scores during RT. However this association is not found between older age and QOL during Chemotherapy. Other issue on which age appeared to have an effect was severity of emesis. In the current study younger age appeared to be one of the risk factors for severe emesis. It seems that younger age patients are more prone to poor QOL during RT. Age above 50 years on the other hand seems to have a protective effect on QOL during RT. Most patients (83.3%) did not score positively on QOL during Chemotherapy irrespective of their age, gender and stage of disease.

3. Concurrent Chemo-RT

Concurrent chemo-RT seems to have a worse affect on QOL during chemotherapy rather than on QOL during RT. Both patients receiving concurrent Chemo-RT scored poorly on QOL during chemotherapy (scores below 5).

4. Long Term Conditions

Only one breast cancer patients indicated presence of a long term condition i.e. Diabetes. Patient with long term condition described their QOL during RT and chemotherapy less positively (with scores of 2,2). Other patients without any long term condition other than cancer such as lung cancer and osteosarcoma patients also scored less positively on QOL questions during chemotherapy and RT. Therefore this link between LTC and poor QOL during Chemotherapy and RT cannot be established strongly due to absence of enough patients with LTC. RT Patient Experience survey also found that patients with Long Term Conditions generally are less likely to describe their RT treatment positively compared to those without LTC [3]. The same survey also found that patients with LTC are less likely to understand benefits and side effects of Radiotherapy. The present study results were not congruent with this finding. It was observed that breast cancer patient BR2 with diabetes scored very positively on the question regarding information about treatment side effects and said she was given information clearly about how to manage and control side effects. This question was not specific to Radiotherapy treatment only. In fact included side effects induced by chemotherapy, radiotherapy and surgery i.e. all the anti cancer treatments a patient has received.

B. Other Analysis

66.7% of patients received patient education (BR1, BR2, BR3, and LG4) and out of these 33.3% received a combination of patient education and psychotherapy (CN5, OS6). No coping skills training or introduction to support groups were offered to cancer patients in this study.

No positive effect could be established between those who received an intervention and who did not in terms of social and physical functioning. Both Patients who received a mix of patient education and psychotherapy reported poor physical and social function. However they reported generally positive scores in terms of QOL in past week despite their severe treatment (amputation in OS6) and advance disease (Advanced stage Ca colon). This could be partly due to patient education and psychotherapy although patient 6 mentioned better patient education is required about the reality he/she faces. Although two Breast cancer patients said that they were not offered any interventions to deal with psycho-social aspects of life it is worth mentioning that they still received patient education about what side effects to expect and how to manage them as shown in the results for efforts to mange treatment side effects. However post-treatment interventions are also required to improve Cancer patients QOL.

It seems that improvement in quality of Life and other psycho-social aspects could be achieved by improving the quality and quantity of the interventions offered to the patients. Use of interventions other than education and psychotherapy are required to improve the QOL such as skills training, emotional support and coping strategies.

V. Role of Various Interventions in Improving QOL of Cancer Patients-Literature Review

Cancer patients in the present study have demanded that interventions need to be introduced to improve their QOL. The patients have also made suggestions regarding interventions that they deem will enhance their QOL and management of treatment induced toxicity. Therefore this section will try to establish the evidence base for various interventions that could be effective in improving cancer patients QOL relapse free Survival especially focusing on interventions such as emotional support, introduction to Support groups, Patient education and counseling. Interventions that can help manage pain, Fatigue, Intractable NV and general QOL will also be briefly discussed as they were some of the toxicities about which either cancer patients were most concerned or they showed high prevalence rate in the present study.

A. Pain

In the present study 66.7% of patients reported G2/3 pain out of which 33.3% of patients reported Grade 3 pain. 33.3% of patients did not answer at all. About 25-30% of newly

diagnosed cancer patients suffer from pain and about 80% of patients having advanced cancer report pain [11]. In the present study it was not possible to establish any connection between advance disease and pain as both patients with advanced disease did not answer the pain toxicity section.

There is also growing evidence of non pharmacological methods being used and tested for pain management in research studies. WHO cancer pain ladder is normally used to manage pain in adults in clinical settings. The WHO ladder has three main steps that include oral administration of drugs round the clock until pain is relieved in the following order: use of Non steroidal anti inflammatory (NSAIDs) drug with or without adjuvant therapy such as paracetamol and aspirin, mild opioids such as codeine with acetaminophen and strong opioids such as Morphine [12], [13]. Adjuvants (additional drugs) are indicated to treat cancer symptoms such as fears and anxiety and neuropathic pain [12], [13]. This three step inexpensive approach has been found to be effective in 80-90% of cases [12]. Recently these percentages have been doubted and it is believed that range is now from 70- 80% [14], [15]. For pediatrics WHO recommends a two step ladder to relieve persistent pain [12]. A modern adaptation of WHO pain ladder has introduced a fourth step that involves neurosurgical procedures such as brain stimulants and invasive techniques such as nerve blocks and neurolysis (thermocoagulation, phenolization, and radiofrequency), surgical interventions to deal with acute pain, chronic non cancer pain and cancer pain [16]. This adaptation of WHO analgesic ladder is also applicable in the management of pediatrics pain, acute pain in emergency departments and in post-operative settings [17].

Adjuvant medication involves antidepressants, anticonvulsants, steroids, ketamine, biphosphonates, anxiolytics, laxatives, hormones, antihistamines and antiemetics [13]. Antidepressants [18], anticonvulsants [19], [20] and steroids [21] can be used to manage cancer related Neuropathic pain.

Among steroids Dexamethasone is commonly administered to relieve spinal cord compression associated pain in IV doses of 10-20mg every 6 hours [21]. Steroids are also used to mange pain associated with soft tissue infiltration and visceral distention, improve appetite, nausea, malaise, and overall quality of life [13]. RT and steroids are used to treat bone pain caused by tumour expansion [13]. Other medications that are considered effective in managing bone pain by inhibiting osteoclast activity include biphosphonates (e.g. Biphosphonates Pamidronate disodium, Zoledronic acid), calcitonin and use of radionuclides (e.g. Strontium-89) for metastatic bone pain [18].

Pharo and Zhou, [13] suggest use of local anaesthetics for non cancerous and malignant neuropathic pain syndrome after failure with trials of antidepressants and anticonvulsants.

Other analgesics include baclofen in the management of spasticity, Trigeminal neuralgia and spinal cord lesion pains [13]. Benzodiazepines are anxiolytics that assist in reducing cancer pain by decreasing patient worries, apprehension and anxiety. Psychostimulants are used to treat opioid- induced sleeplessness, enhance cognition, manage depression, and relieve fatigue. Antihistamines and anticholinergics and antipsychotics and laxatives are used as adjuvants to treat cancer related symptoms such as dizziness, vertigo, nausea and vomiting, delirum, constipation [13]. The review by Pharo and Zhou, [13] concluded that management of cancer pain can be improved by better educating patients, families, health care workers, law enforcement agencies and legislators with all available pharmacological therapeutic modalities.

1. Non Pharmacological Interventions

Non Pharmacological interventions to manage pain can be divided into following categories for ease of understanding their role in treatment of pain: Physical modalities, Psychological interventions, Cognitive Behavourial & Behavourial interventions, psychosocial interventions and complementary medicine [22]. Physical Modalities include exercise, message, Transcutaneous Electrical Stimulation (TENS), Application of heat or cold and rehabilitative treatment [22]. Rehabilitative methods can enhance range of motion, strength, stamina and neuromuscular control thereby decreasing instability and pain linked with disuse [23]. Therapeutic message involves manipulation and therapy of soft tissue by rubbing, kneading and other reflexological handling of soft tissue. A review has shown that message enhances relaxation and improves reduced levels of cortisol and anxiety [24]. A study indicated reduced pain and relaxation in male cancer patients after undergoing a message intervention [25].

A literature review of studies in adult cancer patients with advanced disease receiving palliative care indicated that message interventions showed favourable results with respect to pain, anxiety and depression [26]. Significant reduction in pain was observed [27]-[29] whereas one study failed to show effectiveness of message in terminally ill cancer patients [30]. Message therapy can induce reduced pain lasting up to 18 hours [27], [29]. Reduced pain intensity was observed immediately after message [27]. Two studies showed the effectiveness of message in improving depression [28], [29]. The review concluded that message therapy is cost-effective method for decreasing pain, anxiety and depression in seriously ill cancer patients [28], [30] and is especially indicated in socially isolated patients [31], [32].

2. Complementary and Alternative Medicine Approaches (CAM)

CAM generally includes Hypnosis and meditation programs [22]. Evidence of effectiveness of hypnosis in reducing pain including pain linked with cancer has been found by NIH Technology Assessment panel [33]. Reduction in pain is achieved through cognitive diversion, muscle easing, and modification of perceptions [22]. Hypnosis has been found to be especially useful in decreasing pain associated with surgery or invasive procedures [34].

3. Psychosocial Interventions

Psychosocial interventions of pain include education about cancer, training in coping skills, imagery and hypnosis. Cancer

pain can also be treated by providing education about cancer and pain with a focus on assisting patients to understand pain assessment and to overcome hurdles to treatment of pain, how to use medication in managing pain and how to communicate with health care providers [35], [36]. A randomized trial involving pain education plus brief cognitive Behavourial therapy (academic detailing session about pain management, written instructions for pain and side effects management, how to use a weekly pillbox, how to communicate with physicians about unrelieved pain), resulted in considerable decrease in average, worst and least ratings of pain [37]. A recent randomized control trial of psycho-education in outpatient cancer patients with pain from bone metastasis failed to show efficacy of PRO-SELF pain controlled programme in decreasing pain and opioid intake [38]. The authors associate inadequate psycho-education of patient for possible lack of efficacy.

4. Comprehensive Cognitive Behavioural Therapy (CBT)

This is about learning different pain coping skills such as relaxation, activity pacing, imagery, problem solving, utilization of soothing self statements and communication skills) [35].

A review of behavioural therapies in the management of cancer pain found that comprehensive CBT considerably reduced pain in 46% of the studied analyzed [39]. A study by Dalton and colleagues [40] showed enhanced pain control with the use of comprehensive CBT in patients with advanced cancer. Guided imagery and hypnosis based CBT significantly reduce pain and is especially effective in children receiving painful procedures [41], [42], women with metastatic breast cancer [43] and patients undergoing bone marrow transplant therapy [44].

B. Intractable Vomiting

Intractable vomiting is one of the symptoms about which 1.7 % of cancer patients were highly concerned. This section briefly discusses application of various interventions in the management of this treatment induced symptom.

1. Pharmacological Management

Intractable vomiting can be initially managed by pharmacological monotherapy i.e. use of appropriate single agent antagonist to implicated receptors such as a $5HT_3$ antagonist (e.g. Ondansetron) or less expensive D_2 antagonist [45]. $5HT_3$ antagonists have shown to be effective in managing chemotherapy induced NV [46], radiation induced nausea [47] and post-operative nausea [48]. If monotherapy fails despite appropriate use of antiemetic dosage and around the clock prophylactic administration then use of multiple agents is suggested [45] to block multiple emetic pathways e.g. adding another agent rather than switching agents as it will help block other neurotransmitters which were not controlled or managed by first agent. This is because NV can be caused by action of multiple neurotransmitters at each receptor site and therefore requires use of additional agents to block these neurotransmitters [45]. This approach is evidence based especially in chemotherapy [46], [49] and end of life patients [50].

If symptoms of NV persist then less traditional agents can also be used but evidence encouraging their use remains limited such as use of corticosteroids due to their antiemetic properties [51] or use antidepressants [52] capable of antagonizing 5HT3 receptors to relieve intractable symptoms or use of benzodiazepines to prevent chemotherapy –induced anticipatory nausea [53], [54]. For end of life patients sometimes palliative sedation is also used when all other measures fail to control intractable nausea and vomiting. Prophylactic use of antiemetics is indicated prior to chemotherapy [46], RT [55] and post operative settings [56].

2. Non Pharmacological Management

If symptoms of nausea and vomiting persist then re-evaluation of patient to determine the aetiology of the symptoms is required. Based on the findings of the re-evaluation a number of non pharmacological approaches can be applied such as a botulin toxin injection, dilatation, a proton pump inhibitor, stenting or insertion of PEG tube [57]. Utilization of PEG tube decreases drug costs and re-hospitalizations which is important in hospice settings [58]. A review conducted in 2009 suggested that non-pharmacological interventions should be considered for chemotherapy induced NV [59]. Hypnosis is effective in decreasing anticipatory nausea and vomiting [60]. A randomized controlled trial of Yoga has indicated significant decrease in chemotherapy induced nausea intensity and frequency and intensity of anticipatory vomiting [61].

TABLE VIII
PSYCHO-SOCIAL & PHYSICAL INTERVENTION STUDIES TO MANAGE PAIN, NAUSEA AND VOMITING IN CANCER PATIENTS

Interventions	Studies about Pain	Studies about NV	Outcome
Psych-Ed	Rustoen et al. [38]		Failed to reduce pain
Pt Ed +CBT	Miaskowski et al. [37]		
Comp CBT	Dalton et al. [40]		Enhanced pain control
	Keefe et al. [36]		A review of Com CBT found that comp CBT considerably reduced pain in 46% of the studied analyzed
Imagery, Relaxation, CBT,	Syrjala et al. [44]		Reduces pain in BMT patients
Group Therapy and Hypnosis	Spiegel & Bloom.[43]		Reduces pain in Mets CA Breast patients
Hypnosis based CBT	Liossi & Hatira. [41]; Liossi & Hatira. [42]		Reduces pain in paediatrics undergoing BMT
Hypnosis		Marchioro et al. [60]	Hypnosis is effective in decreasing anticipatory nausea and vomiting
CAM:			
Yoga		Raghavendra et al. [61]	Reduction in Nausea intensity frequency and intensity of anticipatory vomiting

Note: Psys = Psycho-Social Interventions, Pt-Ed=Patient Education, CBT=Cognitive Behavioural Therapy, Comp=Comprehensive, CAM= Complementary and Alternative Medicine, Mets= metastatic, CA=Carcinoma

C. QOL, Emotional Support and Support Groups

In the present study 16.7% of patients feel that emotional support and introduction to support groups will improve their QOL and treatment induced symptoms (see Fig. 16). A study found that patients who do not do well on anxiety and depression scale are more likely to be dissatisfied with the received emotional support [62]. In the present study it has been noted that patients with strong emotional support are more likely to express low scores on home activities, family and social life. They tend to cope better with psychosocial issues such as issues related to family and social life, performing daily activities. The strong emotional support enables them to cope better in all aspects including coping with anxiety and depression due to disease, treatment and its side effects and they are not always dissatisfied with the received emotional support. In fact they regard emotional support from family and friends very important for themselves.

Strong emotional support seems to improve treatment outcome. In the current study Patient BR2 received strong emotional support from family and friends and she scored well on coping with home activities, family and social lives. She had a better treatment outcome than patient BR1 who suffered from recurrence of breast cancer and probably did not have equally strong emotional support. Study by Slevin and colleagues [62] also found that two most important sources for emotional support in view of cancer patients are senior doctors and family and friends. Emotional support from support groups was ranked least important by cancer patients (less than 10%). Among different types of support groups patient are more likely to use doctor and nurse led support groups followed by patients only and patient and family support groups. Psychologist led and Psychiatrist led support groups were less likely to be used by cancer patients i.e. less than 10 % of patients will use psychologist and psychiatrist led support groups [62]. Among informational sources pamphlets were regarded as most important informational source for emotional support followed by TV and books [62], [63] observed that women with improved emotional adjustment regarded their family, doctors and nurses more supportive than women with poor adjustment. Older patients tend to be more satisfied with the emotional support received from health professionals such as senior doctors, radiographer and nurses where as younger patients tend to be more satisfied with emotional support received from family and friends [62]. Cancer patients who receive steady, reliable and strong emotional support tend to adjust effectively over time [64]. The present survey also finds that emotional support from family and health care workers is considered very important by cancer patients and it helps them to cope well with psychosocial issues.

D. Employing Dietary interventions via Patient Counselling to achieve Weight loss & Recurrence Free Survival

A study has shown that dietary interventions are more likely to decrease the risk of recurrence in ER negative than ER positive women with early stage resected breast cancer (p=.15) [65]. Dietary interventions aimed at reducing intake of dietary fat involved 8 bi weekly sessions with nutritionists who counselled patients on lowering dietary fat intake (1 hour duration sessions). The control group also saw nutritionist but was not counselled about dietary fat reduction. The investigational arm has improved relapse free survival (i.e. 24% lower risk of relapse compared to control arm after about a median follow-up of 5 years, p=0.34) but no significant difference was observed in overall survival between the two arms. The experimental arm showed considerable reduction in weight (weight loss of about 6 pounds between groups with p=.005) compared to control arm [65]. More women in control group had Breast conservation Surgery (BCS) than investigation arm and this may have caused a relatively high rate of recurrence in control arm [65]. A multi-institutional randomized trial found that dietary changes such as increase in vegetable, fruit, and fibre and a reduction in dietary fat intake did not reduce recurrence or mortality in previously treated early stage breast cancer patients. Both intervention and control groups experienced 17% recurrence and about 10% mortality rates [66]. The intervention group received intense counselling to adopt the required/tested dietary pattern supplemented with 12 cooking classes in the first year as well as a monthly newsletter throughout the study whereas control group received advice to adopt the 5-A Day Diet.

The results of WINS study [65] are in contrast with results of The Women's Healthy Eating and living (WHEL) Randomized trial [66] in terms of recurrence. Authors attribute differences between these two studies to high proportions of missing dietary intake data in intervention group in WINS study, differential analyses between intervention and control groups (e.g. ER/PR status) in WINS Study, differences between treatment regimen and prognosis between two study groups (WINS and WHEL) [66]. It is important to realize that WHEL study has a longer follow up of about 7 years where as WINS study has a follow up of 5 years. Secondly WHEL patients did not receive chemotherapy. In our opinion the reason for not showing a protective effect in terms of reduced mortality and relapse free recurrence in WHEL investigation arm of breast cancer patients could be due to association of certain vitamins (B2, B6, and Folate) in the diet to increased risk of disease progression. The association between vitamins B2, B6, B7 has been shown to increase disease progression in breast cancer patients in one study [67].

Lee and colleagues [67] has demonstrated that increase in one carbon metabolism related nutrients (B2, Folate) intake is associated with increased Hazard ratio (HR) for disease progression in ER/PR negative in newly diagnosed breast cancer patients compared to a low intake [67]. Poor DFS is indicated in such patients. High intake of Vitamin B6 showed an increased HR for disease progression although the association was not statistically significant [67]. The results of this study are not supported by Swedish Mammography Cohort Study [68] where folate intake has indicated shielding effect on breast cancer specific mortality in ER- patients [68]. Some studies have shown no association of B2, B6 and folate with breast cancer prognosis [69], [70].

E. Psycho-Social Interventions to Improve QOL, Anxiety, Depression and Fatigue during Chemotherapy and Radiotherapy

1. Interventions during RT

A two armed randomized controlled trial investigated the benefits of psychosocial interventions for cancer patients during RT and showed significant improvements on the symptoms of depression, anxiety and health –related QOL (i.e. better overall health status, physical and emotional functioning and decreased insomnia). No significant difference in Financial Difficulties sub scales was observed. No difference was noted in terms of Disease free survival and overall survival between interventional and control groups [71]. The study employed Psych-education, CBT and Supportive Expressive therapy as part of psychosocial interventions that were delivered by a clinician, a nurse and radiation therapist twice weekly in form of a 60 min face to face interview during RT [71].

According to recommendations of a systematic review of 47 RCTs, relaxation techniques alone or in combination with education/skills training, Supportive and supportive expressive therapies are effective in preventing or relieving Anxiety and Depression in Patients undergoing RT. Besides the aforementioned psychosocial interventions, psycho-education and cognitive therapies are recommended in cancer patients undergoing chemotherapy for effective prevention or alleviation of anxiety and depression and depression alone respectively [72].

2. Psychosocial Interventions to Improve QOL and Survival in Patients with Advance and Terminal Cancer

A pilot-randomized trial evaluated the efficacy of CBT interventions in Patients with terminal cancer. The study showed significant improvement in Anxiety in CBT arm but not in control group. However no significant differences were found in Depression and social well being between the two study arms. Self-reported Depression symptoms seemed to decline over time in the entire sample overall. Participants in intervention arm experienced worse physical function due to disease progression and treatment toxicities but improvements in emotional and functional well being [73]. Acceptance and activity pacing based components of CBT interventions might be responsible for improvements in emotional distress and functional well being [73]. Authors of this study suggest that a more depression alleviating approach is required to bring about significant changes in depression / mood by focusing on demoralization and hopelessness as these factors are strongly linked with mood symptoms in this population [73]. The CBT interventions included relaxation skills, coping with cancer fears/doubts and activity pacing were delivered by a licensed clinical psychologist and clinical psychology fellows for about 8 weeks.

Findings of a cluster-randomized control trial were similar to the findings of Greer and colleagues, [73] in terms of reducing anxiety symptoms but not depression in advanced cancer patients receiving palliative treatment in home care setting with the use of CBT Interventions [74].

3. Psychosocial Intervention in Metastatic Breast Cancer Patients to Improve Survival and QOL.

Supportive Expressive Therapy studies have shown mixed results in terms of survival benefits for metastatic breast cancer patients. A RCT showed that supportive expressive group therapy for women with metastatic breast cancer improved QOL including treatment and protection against depression, decreased hopelessness, trauma symptoms and improved social functioning but did not prolong survival [75]. Participants in the intervention arm received SEGT weekly (once a week) plus three classes/week of relaxation therapy for 1 year or more whereas participants in control arm only received three classes/week of relaxation therapy [75]. Another Randomized prospective trial indicated that SEGT is associated with longer survival in ER negative metastatic breast cancer patients but not ER positive patients [76]. Weekly 90 min duration SEGT classes plus educational material (once a week) was offered to participants in intervention arm whereas only weekly educational material was offered to participants in control arm for a minimum of 1 year. The study concluded that SEGT is more effective in metastatic breast cancer patients who are refractory to Hormonal therapy.

The general recommendations for psychosocial care of adults with Cancer from National Breast Cancer Centre and National Cancer Control Initiative Australia [77] can be accessed online and is a good source in selecting evidence based interventions to manage anxiety, depression and other cancer related symptoms. We have avoided citing recommended interventions and practice guidelines from them to prevent any copyright issues.

F. Physical Activity Interventions to Reduce Recurrence, Improve Survival and Enhance QOL

Current cohort studies suggest that physical activity after cancer diagnosis may decrease the risk of recurrence and potentially expand the survival of breast and colorectal cancer survivors by lowering the overall risk of mortality [78]-[81].

In breast cancer patients, moderate level physical activity levels are related with substantially reduced risk of death compared to low activity or no activity [78], [80], [81]. Increasing moderate level physical activity by 60 min / week or more decreases the risk of dying from breast cancer and dying from other causes by 50% in comparison to those breast cancer women who were inactive pre and post diagnosis and had no change whereas reducing the activity level by 60 min or more /week increased the risk of death four-fold in breast cancer women [81].

A randomized trial examining the effects of supervised aerobic exercise on quality of life in women treated for breast cancer reported significantly favourable short term results for social/family well being, functional well being and breast cancer specific concerns with specially encouraging results for physical functioning [82]. Physical functioning is deemed one of the most significant QOL measure in cancer patients and physical function disability is generally associated with high economic costs. Higher physical worth scores and improved

aerobic fitness scores were also reported by both exercise therapy and exercise placebo groups than usual care while insignificant body composition outcomes were observed [82]. The study also reported significantly lower depression score in both exercise therapy and exercise –placebo groups compared to usual care. The study concluded that exercise is more effective in improving QOL in previously inactive breast cancer patients than other QOL improving psychosocial intervention. Three supervised aerobic moderate intensity exercise sessions per week for 8 weeks, with each session of 50 min duration seemed to produce significantly favourable outcomes in terms of QOL aspects in women with breast cancer [82]. Reduced fatigue was also observed.

Another three armed multicentre randomized controlled trial compared aerobic exercise, resistance exercise and usual care for breast cancer patients initiating adjuvant chemotherapy in terms of cancer specific QOL and other psychosocial phenomena reported that neither aerobic nor resistance exercise considerably improved cancer specific QOL in breast cancer patients receiving chemotherapy although trends in fatigue, depression and anxiety favoured exercise groups [83]. However improvement was observed in the categories of self esteem, physical fitness, body composition and chemotherapy completion rate without causing lymphoedema or significant adverse events. Both aerobic and resistance groups were asked to exercise three times / week for the duration of their chemotherapy beginning 1 to 2 week after initiating chemotherapy and ending 3 weeks post chemotherapy [83]. These findings are in contrast to the study performed by Daley and colleagues [82] in terms cancer specific QOL outcomes where depression was significantly reduced in exercise groups. Aerobic fitness achieved better results in terms of self – esteem, conserved aerobic fitness and kept body fat levels whereas resistance exercise improved self esteem, muscular strength and lean body mass and chemotherapy completion rates [83]. The differences between these two studies could be due to the nature of the trial (i.e. one is conducted in post adjuvant setting and other during adjuvant setting, differences in exercise schedule and intensities (e.g. one trial included 8 weeks of exercise interventions whereas other has a median of 17 weeks of exercise intervention period, constant exercise session duration –i.e. 50 min session 3 times a day vs. gradual increase in exercise intensity starting with 15 min session and adding 5 mins at every next session), insufficient adherence, attention effects, assessment of QOL measures using a wide variety of QOL components rather than using specific QOL components such as physical function.

Another trial has reported improved self-esteem and peak oxygen consumption with aerobic exercise in post adjuvant setting rather than during chemotherapy in breast cancer survivors [84]. Improved self esteem is a vital outcome for breast cancer patients undergoing difficult treatments [85].

Three meta analyses of exercise interventions in cancer patients also reported modest effect on fatigue, depression and anxiety and observed that fervent and constant effects emerge in post adjuvant setting [86-88].

1. Complementary and Alternative Medicine (CAM)

Effectiveness of complementary and alternative medicine such as Yoga in breast cancer patients has been reported by a number of studies. A randomized controlled trial investigated the affect of Yoga including physical poses, breathing exercises and meditation on the QOL, fatigue, psychosocial distress and spiritual well being on an ethnically diverse group (African Americans, Hispanics, white) of breasts cancer patients [89]. Significant improvement in social well-being was observed as a whole in women in intervention group compared to control group. Cancer patients not in receipt of chemotherapy appeared to benefit from enhanced emotional well being and mood (decreased distress). Yoga seemed to enhance a sense of social support in the interventional group participants.

A pilot study of Yoga for breast cancer survivors has shown significant differences between intervention and control group at post-intervention in psychosocial aspects (overall QOL, emotional function and diarrhea) [90].

2. Physical Interventions for Prostate Cancer Patients

A randomized control trial of resistance or aerobic exercise in men receiving Radiotherapy for Prostate Cancer [91] showed that fatigue either remained stable or improved in exercise groups. Aerobic exercise produced shot-term effect whereas resistance exercise provided long term improvements in Cancer specific QOL, fatigue, Muscular strength, Triglycerides and Body fat percentage levels during Radiotherapy. Weight increase was not prevented by any of the exercise interventions.

Two other studies also showed less fatigue in men with prostate cancer [92], [93]. One study showed that moderate intensity home based walking carried out for 3 days/week during radiotherapy reduces fatigue [92].

The other study found considerable reduction in fatigue during Androgen deprivation Therapy (ADT) without RT, after 12 weeks of home based exercise [93].

3. Mechanism of Action for Reducing Fatigue and Screening recommendations

Mechanisms for reducing fatigue with exercise may involve enhancing neuromuscular efficiency and decreasing muscular fatigue, decreased depression, improved sleep and increased socialization [94]. Anemia can cause fatigue in cancer patients. Use of erythropoietin in anemic patients is associated with development of thromboembolism [95]. Hence erythropoietin is not indicated in non anemic patients and exercise is a good alternative method to reduce cancer –related fatigue without increasing the risk of embolism [91], [95]. A study has reported that psychosocial interventions do not decrease health care use costs in breast cancer patients [96] and thus alternative QOL interventions such as exercise should be considered.

TABLE IX
PHYSICAL INTERVENTION STUDIES INVOLVING BREAST CANCER PATIENTS ONLY

Study	Setting/Type of Trial	Physical Intervention	Outcome
Holmes et al. [78]	P Obs Study in Stage 1-111 BRCA pts post diagnosis	Physical activities	Reduce risk of death and may improved survival especially in Hormone responsive tumour patients.
Holick et al. [80]	P study in Invasive BRCA,	Recreational physical activities post diagnosis	Decreased overall mortality and breast cancer mortality with increasing overall post-diagnosis recreational physical activity
Irwin et al. [81]	P Obs study in women with Local /regional BRCA	PA pre and post diagnosis	Increased PA post diagnosis is linked with 45% lower risk of death. Reduced PA post Diagnosis is linked with 4 fold increase risk of death
Moadel et al. [89]	RCT	Yoga	Improvement in SW
	Pts without CT	Yoga	Enhanced EW + mood (less distress
Culos-Reed et al. [90]	Pilot study in BRCA survivors	Yoga	Improved overall QOL, EF, Diarrhoea
Courneya et al. [83]	Starting Adjuvant CT/RCT-multicentre	AE/RE	No improvement in Cancer Specific QOL. Trends favoured FT, A, D in EX groups. Improvement in self esteem, physical fitness, body composition and CT completion rate
Daley et al. [82]	RCT in Previously inactive BRCA pts receiving cancer treatment	Supervised AE	Favourable short term results for SW, Family Well being, FW and breast cancer specific concerns with specially encouraging results for PF. Significantly Lower D scores and reduced FT

Note P= Prospective, Obs=Observational, EF= Emotional function, FT=Fatigue, A=Anxiety, D=Depression, FW=Functional Well being, Physical Function = PF, PA= Physical activity, CT=chemotherapy

Australian association for exercise and sport science position stand recommend undertaking of low to moderate intensity exercise 3 -5times per week for at least 20 minutes per session involving aerobic, resistance or mixed exercise types for cancer patients undergoing cancer treatment or those who have completed their treatment [97]. Studies have recommended use of early screening for cancer related fatigue to identify subset of patients who are more likely to develop it [98]-[100]. Screening can be used for cancer related psychological distress to identify high risk patients and to refer them to appropriate interventions [101].

G.Role of Cancer Support Services

There is growing number of cancer survivors and it is important not to ignore their psychosocial needs. Their psychosocial requirements need to be met not only during anti-cancer therapy but also after diagnosis (pre-treatment) and post treatment. An article describing the issues faced by cancer survivors in Australia especially after completion of primary cancer treatment identified psychological, physical, social and existential issues that also included employment problems [102]. Minority of cancer survivors may experience Employment problems in terms of employment discrimination, difficulty with re-entry into work force, dismissal, demotion and lack of career progression and many return to work in diminished capacity [103], [104]. On the top out of pocket medical expenses can further add to adverse socioeconomic and financial difficulties. This might be the case in other countries including Pakistan as in Pakistan there is lack of health insurance and Health benefits. Cancer and its treatment can cause cognitive changes such as reduced learning ability and can hinder the process of returning to work [105]. In Australia a trial of computer-based re-training for cancer survivors has been started to facilitate those who are affected [102]. This is a good initiative and such re-training programmes should be tested and introduced in other parts of the world.

Cancer support services can play an important role in improving the QOL of Cancer Survivors, reduce recurrence and improve survival. Cancer support Services have three focuses. Patient education involving teaching about cancer, available cancer treatment options, methods to manage treatment side effects, long term conditions, associations between cancer and stress, diet, exercise and smoking and learning that long cancer fear lives are possible help decrease stress, fear of dying from cancer, assist in early detection of long term conditions and more efficient self management of acute and long term complications. All this knowledge and information empowers cancer patients to advocate for themselves and assists in bringing about healthy behavioural changes and life styles [106]. Educational services can be made available through internet, telephone and face to face.

The second aim is to coach cancer patients in coping skills to assist them become better accustomed to living with cancer. Coping skills include cognitive behavioural training, stress management, tension-decreasing methods and problem solving for conditions faced by survivors [106] by teaching muscle relaxation, guided imagery, communication and crisis solving skills.

The third focal point of cancer support services is to ensure availability of social and emotional support [106]. It can be achieved by providing a channel for sharing cancer experience with peers and learning from one's peers how to solve many relationship issues encountered by cancer patients such as by using support groups and Supportive Expressive Group therapy. For many cancer patients spending time with their peers can result in reducing feeling of isolation and they also find it easy to discuss their cancer concerns with their peers rather than with family members [106]. Providing guidance to similar other in solving problems from one's own experience can leads to raised self esteem – a feeling of satisfaction of helping someone finding new life purpose [106]. Studies have shown that cancer support services are utilized by small number of patients in USA and Canada and two of the most common reasons for non participation were that people were not aware of the cancer support services and the other reason is lack of recommendation and encouragement from physician to participate in such services [107]-[109].

VI. Recommendations

Most of these recommendations are targeted towards Oncologists, cancer survivors and policy makers in Pakistan but some of the recommendations could also be used by professionals in other parts of the world.

Recommendations I

Effective Pain management can be achieved by adequate educational coaching of patients about cancer and pain, on how to modify their pain management programme, how to communicate with physicians about unrelieved pain and how to use strategies to prevent or treat analgesic side effects. Application of Patient Pain education and comprehensive CBT should be applied to improve pain control in cancer patients.

Recommendation II

Initially Introduce doctor or nurse led support groups as they are more likely to be used by cancer patients. Later on depending on availability of resources introduce Patient only and patient and family support groups as younger patients prefer to use them. Advise patients of the availability of different types of support groups.

Recommendation III

Data on dietary intervention is mixed. Dietary interventions are required to manage some treatment induced side effects such as sore mouth, Esophagitis, weight loss and weight gain etc. Patient counselling can play an important role in introducing dietary changes. Dietary interventions aimed at reducing dietary fat intake seems to have a place in reducing recurrence in ER- Breast cancer patients and therefore should be introduced especially in such patients to improve relapse free survival .

Recommendation IV

Introduce Resistance exercise session during chemotherapy (in adjuvant setting) as it seems to improve self-esteem for breast cancer patients, chemotherapy completing rates, lean body mass and body strength. Encourage cancer survivors to participate in exercise session that are mix of aerobic and resistance exercises in post adjuvant setting as it seems to significantly reduce depression, anxiety and Fatigue. Ideally keep the exercise frequency at least three times a week. Physical activity reduces overall mortality in breast and colorectal cancer patients and reduces recurrence and cancer specific and all cause mortality in breast cancer patients. Introduce resistance exercise session during RT for prostate cancer patients as data shows it improves cancer specific QOL measures, fatigue, aerobic fitness, upper and lower body strength. Introduce screening for cancer related fatigue to identify patients who need cancer related fatigue interventions most.

Recommendation V

Introduce computer based re-training programmes to facilitate the return to work of cancer survivors who have suffered from cognitive changes.

Recommendation VI

Physicians and clinical oncologist should make an effort to encourage and recommend cancer patients to avail cancer support services. They should refer patients to appropriate cancer support services.

Recommendation VII

Introduce the role of oncology nurses specialized in providing psycho-social support to the patients.

Recommendations VIII

Screening should be introduced for symptoms of Pain, Cancer related Fatigue and Tiredness and perhaps for anxiety and Depression so that patients who are at high risk of developing these symptoms can be targeted with effective interventions. Symptoms of intractable vomiting, general weakness, fear of infertility and overall QOL should be better managed.

Recommendation IX

Investment is required by government, hospitals, NGOs, voluntary organizations and International bodies to introduce cancer support services such as introduction of interventions to improve QOL of cancer survivors post diagnosis, during treatment and post treatment and to provide help in dealing with psycho-social issues such as managing at home, social well being, child care, employment and financial difficulties. Investment is also required in improving the current standard of cancer care, cancer support services and for staff training.

VII. Future Directions

Pilot studies and RCTs need to be launched to determine the chemo-RT toxicity profile in patients with various malignancies and Health related QOL especially focusing on cancers other than breast, prostate, and lung as there is lack of studies focusing on less common cancers. Such studies are required for cancer patients in Pakistan as well as worldwide. Future studies need to be directed to determine QOL measures during various phases of cancer pathway. Studies also need to be conducted in determining application and efficacy of various interventions among cancer survivors in Pakistan. Cancer registries need to be established that cover cancer data for entire Pakistan and these registries need to be upgraded in a manner that can help in conducting survivorship studies by exchange of data with the national registries and regional cancer registries (i.e. with registries of other countries).

VIII. Limitation of the Study

One of the limitations of the present study is small number of participants. The other limitation was that 50% of the patients were breast cancer survivors therefore generalization of the findings needs to be done with caution. Although the present study included one less common cancer case i.e. osteosarcoma there needs to be more cases of less common cancers. Despite this limitation the present study has managed to highlight Chemo-RT toxicity profile of breast, lung, colon

and osteosarcoma patients and what these cancer patients believe needs to be done to improve their QOL.

IX. Conclusion

Cancer patients in the present study feel that support groups, better patient education and counselling is required to improve their QOL and management of treatment induced side effects.

High Concerns about Tiredness and Fatigue, Muscular weakness, tense nerves, Pain, intractable vomiting, infertility, amputation, skin discoloration and weak bone were expressed by the study participants. Therefore attention to improved management of these symptoms is warranted. The current study has also showed that QOL of life during RT and especially during chemotherapy was generally poor and thus necessary interventions are required to improve QOL of cancer patients during chemotherapy and RT. Younger age may be the risk factor for severe NV.

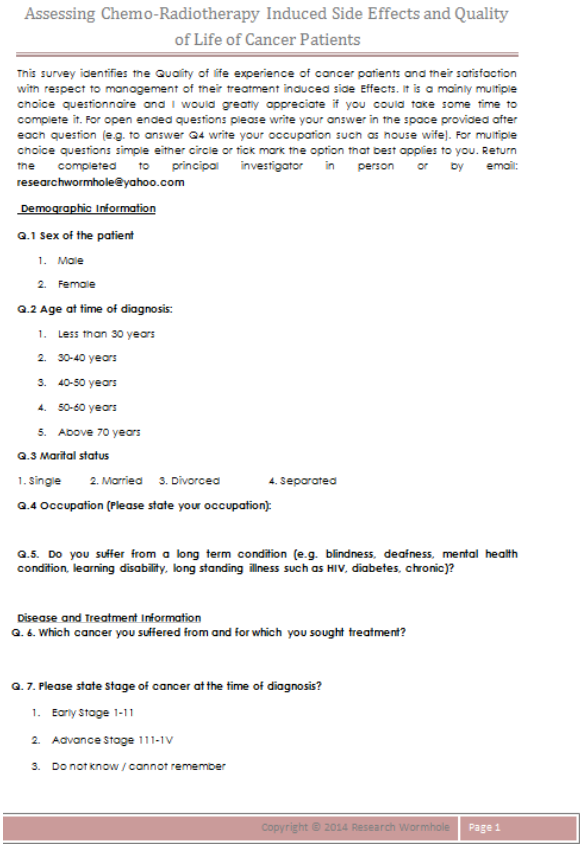
Patients generally showed poor physical function and family and social function. Although 50% of patients had financial difficulty score of 6.5 and below financial issues needs to be addressed. Although 66.7% of cancer patients were offered interventions to deal with their psycho-social needs there is a need to broaden the range of available interventions, their quality and access rate so that every cancer patient who is in need of an intervention have access to this facility.

A number of positive findings were observed during this study in terms of supplying information about managing side effects, efforts made by health care staff to control side effects, patients rating of overall health care support, no occurrence of grade 4 toxicity and moderate availability of interventions to deal with psycho-social needs of cancer patients. The acute chemotherapy toxicity profile showed hair loss, anxiety and depression pain, Tiredness and Fatigue and NV among the worst rated symptoms. The worst rated RT induced toxicities were Tiredness and Fatigue and Pain followed by Peripheral neuropathy and skin changes. Emotional support from family and health care staff is deemed important. Strong family support can improve cancer prognosis.

A number of evidence based recommendations have been made to assist in the selection of appropriate interventions for cancer survivors. When employing cancer support services it is important to include the needs of those who live in rural environment with less facilities at their disposal as well as those who live in urban well off environment. Services delivered through internet such as internet chat rooms or websites may be well received by many people living in big cities but it may not be a successful way of delivering cancer support services in rural and under developed areas with no internet access. Hence cancer support services should be available in various forms to suit not only different living styles (developed and under developed) but also the performance status of cancer patients according to the extent of disease (early, advance, terminal cancer). It is vital to understand cancer and its treatment related symptoms in order to make a case for use of interventions and for better allocation of resources. This study has helped identified the cancer and its treatment induced symptoms that are commonly prevalent among cancer survivors and symptoms which are of most concern to these patients as well as the need for interventions to improve QOL of life of cancer patients in Pakistan. In conclusion present study makes the case for resource allocation to introduce interventions and integrate them in patient's cancer care plan to Improve treatment induced toxicity, QOL of cancer survivors and to deal with their psychosocial issues to enable them better adjust in the society.

Appendix A

Survey Sample Questionnaire



Assessing Chemo-Radiotherapy Induced Side Effects and Quality of Life of Cancer Patients

This survey identifies the Quality of life experience of cancer patients and their satisfaction with respect to management of their treatment induced side effects. It is a mainly multiple choice questionnaire and I would greatly appreciate if you could take some time to complete it. For open ended questions please write your answer in the space provided after each question (e.g. to answer Q4 write your occupation such as house wife). For multiple choice questions simple either circle or tick mark the option that best applies to you. Return the completed to principal investigator in person or by email: **researchwormhole@yahoo.com**

Demographic Information

Q.1 Sex of the patient

1. Male
2. Female

Q.2 Age at time of diagnosis:

1. Less than 30 years
2. 30-40 years
3. 40-50 years
4. 50-60 years
5. Above 70 years

Q.3 Marital status

1. Single 2. Married 3. Divorced 4. Separated

Q.4 Occupation (Please state your occupation):

Q.5. Do you suffer from a long term condition (e.g. blindness, deafness, mental health condition, learning disability, long standing illness such as HIV, diabetes, chronic)?

Disease and Treatment Information

Q. 6. Which cancer you suffered from and for which you sought treatment?

Q. 7. Please state Stage of cancer at the time of diagnosis?

1. Early Stage 1-11
2. Advance Stage 111-1V
3. Do not know / cannot remember

Copyright © 2014 Research Wormhole Page 1

1. Cure
2. Palliation of symptoms
3. Do not know / Cannot remember

Q. 9. Select the treatments that you received for your cancer?

1. Chemotherapy
2. Radiotherapy
3. Hormone Therapy
4. Surgery
5. Biological therapy
6. Other: (Please specify)

Q.10. Did you receive chemotherapy and radiotherapy treatment concurrently (i.e. at the same time/simultaneously)?

1. Yes 2. No

Q. 11. If you received chemotherapy how long the course was?

1. 3 weeks
2. 5 weeks
3. Other: please specify:----------
4. Do not know / cannot remember

Q.12. Are you having any long-term side effects due to chemotherapy and radiotherapy treatment? Please state them in the relevant box.

Chemotherapy Long term Effects	Radiotherapy long term Effects

Q. 13. If you received Radiotherapy what was the duration of treatment?

Total Treatment duration in weeks	No of attendances or visits (treatments) per day	Total dose
1	1	20Gy
5	1	45-50Gy
6	1	60-70Gy
Other:	Other:	Other:

Chemo-Radiation Induced Acute Morbidity and Toxicity

Q.14. Which Radiotherapy and chemotherapy induced treatment side effects you encountered? Please indicate the extent to which you experienced these side effects or problems during radiotherapy by selecting a number between 0 to 4.

Radiation-Side Effects	Chemo-Side Effects	Grading 0=No, 1=mild, 2=moderate, 3=Severe, 4= Complete loss of function
Skin changes (e.g. dry, redness, itchy, flaky)	Skin changes (e.g. dryness, redness, itchy, flaky)	
Tiredness & fatigue	Tiredness & fatigue	
Pain	Pain	
Appetite loss	Appetite loss	
Hair loss	Hair loss	
Difficulty Sleeping	Difficulty Sleeping	
Constipation	Constipation	
Nausea / vomiting	Nausea / vomiting	
Diarrhoea	Diarrhoea	
Shortness of breath	Shortness of breath	
Esophagitis/difficulty in swallowing	Esophagitis/difficulty in swallowing	
Tissue Fibrosis	Tissue Fibrosis	
Mouth ulcer/soreness	Mouth ulcer/soreness	
Difficulty in breathing &	Difficulty in breathing & dry	
dry cough	cough	
Urinary problems	Urinary problems	
Bowel problems	Bowel problems	
Anxiety & Depression	Anxiety & Depression	
Drowsiness	Drowsiness	
Peripheral Neuropathy	Peripheral Neuropathy	
Others: Please specify	Others: Please specify	

Psychosocial Issues and Quality of Life

For following questions please circle the number between 1-10 that best applies to you:

Q. 15. How would you describe the quality of life during the radiotherapy treatment?

Extremely poor 0 1 2 3 4 5 6 7 8 9 10 Excellent

Q. 16. How would you describe your quality of life during chemotherapy treatment?

Extremely poor 0 1 2 3 4 5 6 7 8 9 10 Excellent

Q. 17. How good was your quality of life in the past week?

Extremely poor 0 1 2 3 4 5 6 7 8 9 10 Excellent

Q. 18. How hard it is for you to cope today as a result of your treatment?

Not at all difficult 0 1 2 3 4 5 6 7 8 9 10 very difficult

Q. 19. To what extent your treatment and disease affected your activities at home?

No problem 0 1 2 3 4 5 6 7 8 9 10 severe problem

Q. 20. Has your physical condition and treatment hindered your family and social life?

Not at all 0 1 2 3 4 5 6 7 8 9 10 very much

Q.21. Which treatment related side effect you are most concerned about?

Q. 22. How much financial burden have you incurred as a result of your disease and treatment

None 0 1 2 3 4 5 6 7 8 9 10 great deal

Information about Support and Quality of Life

For Following questions please circle the answer that best applies to you:

Q.23. Were you told how to manage or control your side effects by a doctor, nurse, radiographer or any member of health care staff?

1. Clearly, 2. to some extent, 3. No, 4. Do not know/do not remember

Q.24. Did staff do everything possible to control the side effects?

1. Yes
2. No

Q.25. Do you use any medication to manage / control any of the treatment induced side effects?

1. Yes 2. No

If Yes which medication you use and how often you use it----------

Q. 26. How do you rate the overall health care support that you received during and after your treatment?

Excellent, very good, good, fair, poor, very poor

Q.27. Were you offered support to deal with psychosocial aspects of your treatment and its side effects (i.e. to control stress, depression, feeling of social isolation)

1. Introduction to cancer support groups (e.g. Social support groups)
2. Patient education
3. Psychotherapy
4. Coping skills training
5. Any other: (Please specify)----------
6. No psychosocial intervention was offered

Q.28. How do you think patient's quality of life and management of treatment side effects can be improved?

Thank you again for answering these questions.

Fig. 17 Survey Sample Questionnaire

APPENDIX B

Chemotherapy Course Duration

Case BR1 said the chemotherapy Course was 3 weeks long. However the patient also mentioned receiving 4 cycles of

chemo. Therefore we assume she meant total of 4 cycles of chemotherapy with 3 weeks gap after each cycle. Similarly Patient BR3 (a case of advanced stage breast cancer with curative intent of treatment) said that she received 3weeks of chemotherapy course. She could have meant receiving 1 cycle of chemo every 3 weeks or total 3 cycles. Hence we stick to 1 cycle that is followed by 3 weeks gap. This might not be the case as breast patients usually get 3- 6 cycles of chemo unless this patient has just started her treatment. Patient LG4 (Early stage lung cancer with curative treatment aim) said that chemo course was 3 months long. This patient also had surgery. It may be possible that this patient had 4 treatments of chemotherapy leading to a full course of 3 months. Therefore 4 cycles are assumed for this patient. Patient CN5 said he received 8 cycles of chemotherapy with 3 weekly gaps. Patient 6OS (A case of early stage Osteosarcoma of right leg with curative treatment intent) said he received 5 weeks of chemotherapy course. It is assumed that this patient may have received 1 cycle of chemo i.e. 1 cycle every 35 days (5 weeks). For this study the number of cycles is kept to 1 as patient only mentioned 5 weeks (i.e. 35 days)

APPENDIX C

Chemotherapy Induced Acute Toxicity Results

This section describes full results for Chemotherapy Induced acute Toxicity in terms of absolute numbers and percentages. Total number of patients is 6. The missing information refers to respondents who did not reply to a partcular question or toxicity. Some patients indicated the presence of the toxicity by tick marking it but failed to grade the toxicity. These patients were designated as PN (Toxicity/symptom present but not graded). The number of PN respondents were included in claculating total/overall percenatge for that symptom /toxicity e.g. in case of NV 4 patients graded NV symptom however one patient maked it but did not grade it (PN). Thus in total 5 patients experienced the toxicity giving rise to a percenatge value of 83.3%. This also means that in such cases the individual percenatges will not add up to total percentage. As no grade 4 toxiciticies were observed they have been omitted from results section.

TABLE X
HAIR LOSS, ANXIETY & DEPRESSION AND PAIN

Chemo	Respondents (total no)	Percentage
Hair loss	5	83.3%
Missing	1	16.7%
Grade 0	0	0%
Grade 1	0	0%
Grade 2	0	0%
Grade 3	4	66.7%
Grade0/1	**0**	**0%**
Grade 2/3	**4**	**66.7%**
Anxiety & Depression	5 (1 patient ticked but did not grade it)	83.3%
Missing	1	16.7%
Grade 0	0	0%
Grade 1	0	0%
Grade 2	1	16.7%
Grade 3	3	50%
Grade 0/1	**0**	**0%**
Grade 2/3	**4**	**66.7%**
Pain	4	66.7%
Missing	2	33.3%
Grade 0	0	0%
Grade 1	0	0%
Grade 2	2	33.3%
Grade 3	2	**33.3%**
Grade 0/1	**0**	**0%**
Grade2/3	**4**	**66.7%**

TABLE XI
TIREDNESS & FATIGUE, NV AND INSOMNIA

Chemo	Respondents (Total no)	Percentage
Tiredness and fatigue	3	50%
Missing	3	50%
Grade 0	0	0%
Grade 1	0	0%
Grade 2	1	16.7%
Grade 3	2	**33.3%**
Grade 0/1	**0**	**0%**
Grade 2/3	**3**	**50%**
Nausea & Vomiting	5 (1 patient ticked but did not grade it)	83.3%
Missing	1	16.7%
Grade 0	1	16.7%
Grade 1	0	0%
Grade 2	2	33.3%
Grade 3	1	16.7%
Grade 0/1	**1**	**16.7%**
Grade 2/3	**3**	**50%**
Insomnia	4	66.7%
Missing	2	33.3%
Grade 0	1	16.7%
Grade 1	1	16.7%
Grade 2	0	0%
Grade 3	2	**33.3%**
Grade 0/1	**2**	**33.3%**
Grade2/3	**2**	**33.3%**

TABLE XII
LOWER GI TOXICITY

Lower GI Tract Toxicities	Respondents (Total no)	Percentage
Constipation	3	50%
Missing	3	50%
Grade 0	2	33.3%
Grade 1	0	0%
Grade 2	1	16.7%
Grade 3	0	0%
Grade0/1	**2**	**33.3%**
Grade 2/3	**1**	**16.7%**
Diarrhoea	3	50%
Missing	3	50%
Grade 0	2	33.3%
Grade 1	0	0%
Grade 2	1	16.7%
Grade 3	0	0%
Grade 0/1	**2**	**33.3%**
Grade 2/3	**1**	**16.7%**
Urinary Problems	4	66.7%
Missing	2	33.3%
Grade 0	4	66.7%
Grade 1	0	0%
Grade 2	0	0%
Grade 3	0	0%
Grade 0/1	**4**	**66.7%**
Grade 2/3	**0**	**0%**
Bowel Problems	4	66.7%
Missing	2	33.3%
Grade 0	3	50%
Grade 1	1	16.7%
Grade 2	0	0%
Grade 3	0	0%
Grade 0/1	**4**	**66.7%**
Grade 2/3	**0**	**0%**

TABLE XIII
RESPIRATORY TOXICITY

Respiratory Toxicities	Respondents (total no)	Percentage
Shortness of Breath	**4**	**66.7%**
Missing	2	33.3%
Grade 0	3	50%
Grade 1	0	0%
Grade 2	1	16.7%
Grade 3	0	0%
Grade 0/1	**3**	**50%**
Grade 2/3	**1**	**16.7%**
Difficulty in Breathing	5 (1 patient ticked but did not grade it)	83.3%
Missing	1	16.7%
Grade 0	3	50%
Grade 1	0	0%
Grade 2	1	**16.7%**
Grade 3	0	0%
Grade 0/1	**3**	**50%**
Grade 2/3	**1**	**16.7%**
Dry Cough	5 (1 patient ticked but did not grade it)	83.3%
Missing	1	16.7%
Grade 0	2	33.3%
Grade 1	2	33.3%
Grade 2	0	0%
Grade 3	0	0%
Grade 0/1	**4**	**66.7%**
Grade 2/3	**0**	**0%**

TABLE XIV
UPPER GI TRACT TOXICITY

Upper GI tract Toxicities	Respondents (Total no)	Percentage
Esophagitis	3	50%
Missing	3	50%
Grade 0	2	33.3%
Grade 1	0	0%
Grade 2	1	16.7%
Grade 3	0	0%
Grade 0/1	**2**	**33.3%**
Grade 2/3	**1**	**16.7%**
Mouth Ulcer/soreness	3	50%
Missing	3	50%
Grade 0	2	33.3%
Grade 1	0	0%
Grade 2	1	**16.7%**
Grade 3	0	0%
Grade 0/1	**2**	**33.3%**
Grade 2/3	**1**	**16.7%**
Appetite Loss	3	50%
Missing	3	50%
Grade 0	0	0%
Grade 1	0	0%
Grade 2	2	33.3%
Grade 3	1	16.7%
Grade 0/1	**0**	**0%**
Grade2/3	**3**	**50%**

APPENDIX D

Glossary

Cancer Survivor: Anyone diagnosed with cancer from time of diagnosis until death.

Complementary and Alternative Medicine (CAM): A term that encompasses both traditional medicine (e.g. Chinese medicine, Indian Ayruveda, Arabic Unani) and indigenous medicine as well as use of non medication therapies (e.g. acupuncture, meditation, message)

Coping: A complicated mental process, by which a person handles stress, resolves problems and makes decisions.

Relapse Free Survival: time to cancer recurrence at any site (in context of WINS study).

Quality of Life: Quality of an individual's daily life (well-being of patient). It includes impact of treatment and its side effects on a patient's quality of life.

ACKNOWLEDGEMENT

Thanks to all participants of this survey whose responses are highly valued.

No conflict of Interest exists. The research was carried out independently by the researcher.

REFERENCES

[1] International Agency for Research on Cancer and WHO Press release No 223, "Latest World Cancer statistics," 2013. Available at: http://www.iarc.fr/en/media-centre/pr/2013/pdfs/pr223_E.pdf. (Accessed 02/01/2015)

[2] Cancer Therapy Evaluation Program, "Common Toxicity Criteria Ver 2," 1999. Available at: http://prevention.cancer.gov/files/clinical-trials/common-toxicity-criteria.pdf. (Accessed 25/12/2014)

[3] Quality Health, "Radiotherapy Patient Experience Survey 2013 National Report," 2013. Available at: http://www.sor.org/system/files/

news_story/201401/radiotherapy_patient_experience_survey_2013_national_report.pdf. (Accessed 25/12/2014).

[4] C. Booth, M. Clemon, G. BPharm, A. Joy, S. Young, W. Callaghan, et al., "Chemotherapy Induced Nausea and Vomiting in Breast Cancer Patients: A prospective Observational study," *The Journal of Supportive Oncology, 5, 374-380, 2007.*

[5] P. Chambers, and S. Daniels, "Antiemetic Guidelines for Adult Patients receiving Chemotherapy and Radiotherapy," 2010. Available at: http://www.londoncancer.org/media/65597/antiemetic-guidelines-november-2010.pdf. (Accessed 25/12/2014).

[6] A. Bhal, D. Sharma, P. Julka, and G. Rath, "Chemotherapy related toxicity in locally advanced non-small cell lung cancer," *Journal of Cancer Research and Therapeutics*, 2, 14-16, 2006. Available at: http://www.cancerjournal.net/article.asp?issn=0973-1482;year=2006;volume=2;issue=1;spage=14;epage=16;aulast=Bahl. (Accessed 25/12/2014).

[7] A. Nowak, M. Stockler, and M. Byrne, "Assessing Quality of Life during chemotherapy for Pleural Mesothelioma: Feasibility, Validity and Results of Using the European Organization for Research and Treatment of Cancer Core Quality of Life questionnaire and Lung Cancer Module," *Journal of Clinical Oncology.*, 22, 3172-3180, 2004.

[8] W. Pril, "Evidence report on the occurrence, assessment, and treatment of depression in cancer patients," *Journal of the National Cancer Institute. Monographs*, 32, 32–9, 2004.

[9] D. Stark, and A. House, "Anxiety in cancer patients," *British Journal of Cancer*, 83, 1261–7, 2000. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2408796/pdf/83-6691405a.pdf. (Accessed 25/12/2014)

[10] D. Cella, K. Davis, W. Breitbart G. Curl, and Fatigue Coalition, "Cancer-related fatigue: Prevalence of proposed diagnostic criteria in a United States sample of cancer survivors," *Journal of Clinical Oncology*, 19, 3385–3391, 2001.

[11] P. G. Fine, "The evolving and important role of anesthesiology in palliative care," *Anesthesia Analgesia*, 100,183–188, 2005.

[12] WHO, "WHO's Cancer Pain ladder for adults," Available at: http://www.who.int/cancer/palliative/painladder/en/. (Accessed 9/12/2014).

[13] G. Pharo, and D. Zhou, "Pharmacological Management of Pain," *JAOA*, 105, S21-S28, 2005.

[14] M. Lema, "Invasive procedures for cancer pain," *Pain Clin Update*, 6, 1-8, 1998.

[15] Y. Kanpolat, "Percutaneous destructive pain procedures on the upper spinal cord and brain stem in cancer pain: CT-guided techniques, indications and results," *Advances and Technical Standards in Neurosurgery*, 32, 147-73, 2007.

[16] R. Miguel, "Interventional treatment of cancer pain: The Fourth Step in the World Health Organization Analgesic Ladder?," *Cancer Control*, 7, 149-56, 2000. Available at: http://www.medscape.com/viewarticle/408976. (Accessed 9/12/2014)

[17] G. Vargas-Schaffer, "Is the WHO Analgesic ladder still valid?," *Canadian Family Physician*, 56, 514-7, 2010. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2902929/ Accessed 9/12/2014

[18] D. Carr, L. Goudas, E. Balk, R. Bloch, J. Ionnidis, and J. Lau, "Evidence report on the treatment of pain in cancer patients," *Journal of the National Cancer Institute. Monographs*, 32, 23–31, 2004.

[19] E. Dunteman, "Levetiracetam as an adjunctive analgesic in neoplastic plexopathies: case series and commentary," *Journal of Pain & Palliative Care Pharmacotherapy*, 19, 35–43, 2005.

[20] H. Adriaensen, K. Plaghki, C. Mathieu, A. Joffro, and K. Vissers, "Critical review of oral drug treatments for diabetic neuropathic pain—clinical outcomes based on efficacy and safety data from placebo-controlled and direct comparative studies," *Diabetes Metab Res Rev*, 21, 231–240, 2005.

[21] P. Demoly, and K. Chung, "Pharmacology of corticosteroids," *Respir Med*, 92, 385–394, 1998.

[22] L. Pujol, and D. Monti, "Managing Cancer Pain with Non Pharmacologic and Complimentary Therapies," *JAOA.*, 107, ES15-ES21

[23] S. Willick, S. Herring, and J. Press, "Basic concepts in biomechanics and musculoskeletal rehabilitation," In: J. Loeser, S. Bugler, C. Chapman, C. Turk, eds. *Bonica's Management of Pain*. 3rd ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2001, 1815-1831.

[24] T. Field, "Massage therapy effects," The *American Psychologist*, 53,1270-1281, 1998.

[25] S. Weinrich, and M. Weinrich, "The effect of massage on pain in cancer patients," *Applied Nursing Research*. 3, 140-145, 1990.

[26] M. Falkensteiner, F. Mantovan, I. Muller, and C. Them, "The Use of Message Therapy for reducing pain, Anxiety and depression in Oncological palliative care patients: A narrative review of the Literature," *International Scholarly Research Network Nursing*, 2011 Available at: http://www.hindawi.com/journals/isrn/2011/929868/. Accessed 11/12/2014.

[27] D. Wilkie, J. Kampbell, S. Cutshall et al., "Effects of massage on pain intensity, analgesics and quality of life in patients with cancer pain: a pilot study of a randomized clinical trial conducted within hospice care delivery," *The Hospice Journal*, 15, pp. 31–53, 2000.

[28] A. Cassileth and A. Vickers, "Massage therapy for symptom control: outcome study at a major cancer center," Journal of Pain and Symptom Management, 28, pp. 244–249, 2004.

[29] J. Kutner, M. Smith, L. Corbin, L. Hemphill, K. Benton, B. Mellis, et al., "Massage therapy versus simple touch to improve pain and mood in patients with advanced cancer: a randomized trial," *Annals of Internal Medicine*, 149, 369–379, 2008. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2631433/. (Accessed 26/12/2014)

[30] L. Downey, P. Diehr, L. Standish D. Patrick, L. Kozak, D. Fisher et al., "Might massage or guided meditation provide "means to a better end"? Primary outcomes from an efficacy trial with patients at the end of life," *Journal of Palliative Care*, 25, 2, 100–108, 2009. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2858762/pdf/nihms-189022.pdf. (Accessed 26/12/2014)

[31] N. Russell, S. Sumler, C. Beinhorn, and M. Frenkel, "Role of massage therapy in cancer care," *The Journal of Alternative and Complementary Medicine*, 14, 209– 214, 2008.

[32] S. Nagele and A. Feichtner, "Lehrbuch der Palliativpflege," Facultas, Wien, Austria, 2005

[33] "Integration of behavioural and relaxation approaches into the treatment of chronic pain and insomnia. NIH Technology Assessment Panel on Integration of Behavioural and Relaxation Approaches into the Treatment of Chronic Pain and Insomnia," *JAMA*, 276, 313-318, 1996.

[34] G. Montgomery, C. Weltz, M. Seltz, and D. Bovbjerg, "Brief presurgery hypnosis reduces distress and pain in excisional breast biopsy patients," The *International Journal of Clinical and Experimental Hypnosis*, 50, 17-32, 2002.

[35] International Association for the Study of Pain, "Global Year against Pain, Psychosocial Interventions for Cancer Pain," 2008. Available at: http://www.iasppain.org/files/Content/ContentFolders/GlobalYearAgainstPain2/CancerPainFactSheets/PsychosocialInterventions_Final.pdf. (Accessed 11/12/2014)

[36] F. Keefe, A. Abernethy, and L. Campbell, "Psychological approaches to understanding and treating disease-related pain," *Annu Rev Psychol*, 56:601-630, 2005.

[37] A. Miaskowski, M. Dodd, C. West, K. Schumacher, S. Paul, D. Tripathy, and P. Koo, "Randomized clinical trial of the effectiveness of a self-care intervention to improve cancer pain management," *Journal of Clinical Oncology*, 22, 1713–20, 2004.
T. Rustoen, B. Valeberg, E. Kolstad, E. Wist, S. Paul, and C. Miaskowski, "A randomized clinical trial of the efficacy of a self care Intervention to improve cancer pain management," *Cancer Nursing*, 37, 34-43, 2014.

[38] T. Rustoen, B. Valeberg, E. Kolstad, E. Wist, S. Paul, and C. Miaskowski, "A randomized clinical trial of the efficacy of a self care Intervention to improve cancer pain management," *Cancer Nursing*, 37, 34-43, 2014.

[39] A. Abernethy, F. Keefe, D. McCrory, C. Scipio, and D. Matchar, "Behavioral therapies for the management of cancer pain: a systematic review," In: H. Flor, E. Kalso, J. Dostrovsky, editors. *Proceedings of the 11th World Congress on Pain*. Seattle: IASP Press, 2006, 789–798

[40] J. Dalton, F. Keefe, J. Carlson, and R. Youngblood, "Tailoring cognitive-behavioural treatment for cancer pain," *Pain Management Nursing*, 5, 3–18, 2004.

[41] A. Liossi, and P. Hatira, "Clinical hypnosis versus cognitive behavioural training for pain management with pediatric cancer patients undergoing bone marrow aspirations," The International Journal of Clinical and Experimental Hypnosis, 47, 104–16, 1999.

[42] C. Liossi, and P. Hatira, "Clinical hypnosis in the alleviation of procedure-related pain in pediatric oncology patients," The *International Journal of Clinical and Experimental Hypnosis*, 51:4–28, 2003.

[43] A. Spiegel, and J. Bloom, "Group therapy and hypnosis reduce metastatic breast carcinoma pain," *Psychosomatic Medicine*, 45, 333–9, 1983. Available at: http://bscw.rediris.es/pub/bscw.cgi/d4999766/Spiegel-Group_therapy_hypnosis_reduce_metastatic_breast_carcinoma_pain.pdf. (Accessed 26/12/2014).

[44] K. Syrjala, G. Donaldson, M. Davis, M. Kippes, and J. Carr, "Relaxation and imagery and cognitive-behavioral training reduce pain during cancer treatment: a controlled clinical trial," *Pain*, 1995, 63, 189–98, 1995.

[45] A. Wood, J. Sega, B. Lynch, and J. Roenn, "Mangement of intractable Nausea and vomiting in patients at the end of life," *JAMA*, 298, 1196-1207, 2007.

[46] M. Kris, P. Hesketh, M. Somerfield, P. Feyer, R. Clark-snow, J. Koeller, et al., "American Society of Clinical Oncology guideline for antiemetics in oncology: update 2006," *Journal of Clinical Oncology*, 24, 2932-2947, 2006. Available at: http://jco.ascopubs.org/content/24/18/2932.full.pdf. (Accessed 26/12/2014)

[47] J. Roberts, and T. Priestman, "A review of ondansetron in the management of radiotherapy- induced emesis," *Oncology*, 50, 173-179, 1993.

[48] T. Gan, T. Meyer, C. Apfel, F. Chung, P. Davis, S. Eubanks, et al., "Consensus guidelines for managing postoperative nausea and vomiting," *Anesthesia and Analgesia*, 97, 62-71, 2003.

[49] K. Mystakidou, S. Befon, C. Liossi, and L. Vlacho, "Comparison of tropisetron and chlorpromazine combinations in the control of nausea and vomiting of patients with advanced cancer," *J Pain Symptom Manage*, 15, 176-184, 1998.

[50] R. Cole, F. Robinson, L. Harvey, K. Trethowan, and V. Murdoch, " Successful control of intractable nausea and vomiting requiring combined ondansetron and haloperidol in a patient with advanced cancer," *J Pain Symptom Manage*, 9, 48-50, 1994.

[51] S. Grunberg, R. Deuson, P. Mavros, O. Geling, M. Hansen, G. Cruciani et al., "Incidence of chemotherapy induced nausea and emesis after modern antiemetics," *Cancer*, 100, 2261-2268, 2004. Available at: http://onlinelibrary.wiley.com/doi/10.1002/cncr.20230/pdf. (Accessed 26/12/2014)

[52] D. Theobald, K. Kirsh, E. Holtsclaw, K. Donaghy, and S. Passik, "An open-label, crossover trial of mirtazapine (15 and 30 mg) in cancer patients with pain and other distressing symptoms," *J Pain Symptom Manage*, 23, 442-447, 2002.

[53] A. Malik, W. Khan, M. Qazilbash, E. Ata, A. Butt, and M. Khan, "Clinical efficacy of lorazepam in prophylaxis of anticipatory, acute, and delayed nausea and vomiting induced by high doses of cisplatin," *American Journal of Clinical Oncology*, 18, 170-175, 1995.

[54] S. Simms, V. Rhodes, and R. Madsen, "Comparison of prochlorperazine and lorazepam antiemetic regimens in the control of postchemotherapy symptoms," *Nursing Research*, 42, 234-239, 1993.

[55] T. Priestman, J. Roberts, H. Lucraft, C. Collis, M. Adams, B. Upadhyaya et al., "Results of a randomized, double blind comparative study of ondansetron and metoclopramide in the prevention of nausea and vomiting following high-dose upper abdominal irradiation," *Clinical Oncology (R Coll Radiol)*, 2, 71-75, 1990.

[56] M. Burmeister, T. Standl, M. Wintruff, P. Brauer, I. Blanc, J. Schulte am Esch, "Dolasetron prophylaxis reduces nausea and postanaesthesia recovery time after remifentanil infusion during monitored anaesthesia care for extracorporeal shock wave lithotripsy," *Br J Anaesth*, 90, 194-198, 2003.

[57] B. Brücher, H. Stein, H. Bartels, H. Feussner, J. Siewert, "Achalasia and esophageal cancer: incidence, prevalence, and prognosis," *World Journal of Surgery*, 25, 745-749, 2001.

[58] M. Gupta, M. Davis, S. LeGrand, D. Welsh, R. Lagman, "Nausea and Vomiting in Advanced cancer: the Cleveland Clinic Protocol," *The Journal of Supportive Oncology*, 11, 8-13, 2013.

[59] D. Salvia, P. Reis, I. Gomes, S. Funghetto, C. Leon, "Non Pharmacological Interventions for chemotherapy Induced Nausea and Vomits: Integrated review," Online Brazilian Journal of Nursing, 8, 2009. Available at: http://www.objnursing.uff.br/index.php/nursing/article/view/j.1676-4285.2009.2098/463 (8/12/2014).

[60] A. Marchioro, G. Azzarello, F .Viviani, F. Barbato, M. Pavanetto, F. Rosetti F, et al., "Hypnosis in the Treatment of Anticipatory Nausea and Vomiting in Patients Receiving Cancer Chemotherapy," *Oncology*, 59 100-104, 2000.

[61] R. Raghavendra, R. Nagarathna, H. Nagendra, K. Gopinath, B. Srinth, B. Ravi, et al., "Effects of an integrated yoga program on chemotherapy-induced nausea and emesis in breast cancer Patients," *European Journal of Cancer Care*, 16, 462-474, 2007.

[62] A. Slevin, S. Nichols, S. Downer, P. Wilson, T. Lister, S. Arnott, et al., "Emotional support for cancer patients: What do patients really want?," *British Journal of Cancer*, 74, 1275-1279, 1996.

[63] K. Jamison, D. Wellisch, and R. Pasnau, "Psychosocial Aspects of mastectomy: 1. The women's perspective," *The American. Journal of Psychiatry*,, 34, 432-436, 1978.

[64] C. Dunkel-Schetter, "Social Support and Cancer: Findings based on patient interviews and their implications," *Journal of Social Issues*, 40, 77-98, 1984.

[65] R. Chlebowski, G. Blackburn, C. Thomson, D. Nixon, A. Shapiro, M. Hoy, et al., "Dietary fat reduction and breast cancer outcome: Interim efficacy results from the Women's Intervention Nutrition Study,". *Journal of the National Cancer Institute*, 98, 1767-76, 2006.

[66] J. Pierce, L. Natarajan, B. Caan, B. Parker, E. Greenberg, S. Flatt, et al., "Influence of a Diet Very High in Vegetables, Fruit, and Fibre and Low in Fat on Prognosis Following Treatment for Breast Cancer: The Women's Healthy Eating and Living (WHEL) Randomized Trial," *JAMA*, 18, 289-98, 2007. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2083253/. (Accsessed 8/12/2014)

[67] Y. Lee, S. Lee, J. Choi, M. Song, H. Sung, S. Jeon, et al., "Prognosis of breast cancer is associated with one carbon metabolism related nutrients among Korean women," *Nutrition Journal*, 11, 1-9, 2012. Available at: http://www.nutritionj.com/content/pdf/1475-2891-11-59.pdf. (Accessed 8/12/2014).

[68] A. Harris, L. Bergkvist, and A. Wolk, "Folate intake and breast cancer mortality in a cohort of Swedish women," Breast Cancer Research and Treatment, 132, 243–250, 2011. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3747350/. (Accessed 26/12/2014)

[69] M. Holmes, M. Stampfer, G. Colditz, B. Rosner, D. Hunter, and W. Willett, "Dietary factors and the survival of women with breast carcinoma," *Cancer*, 86, 826–835, 1999.

[70] E. Rossi, J. Hung, J. Beilby, M. Knuiman, M. Divitini, and H. Bartholomew, "Folate levels and cancer morbidity and mortality: prospective cohort study from Busselton, Western Australia," *Annals of Epidemiology*, 16, 206–212, 2006.

[71] Z. Guo, H. Tang, H. Li, S. Tan, K. Feng, Y. Huang, et al., "The Benefits of psychosocial interventions for Cancer patients undergoing Radiotherapy," *Health and Quality of Life outcomes*, 11, 1-12, 2013. Available at: http://www.hqlo.com/content/pdf/1477-7525-11-121.pdf. (Accessed 26/12/2014)

[72] P. Jacobsen, K. Donovan, Z. Swaine, et al., "Management of anxiety and depression in adult cancer patients: toward an evidence-based approach," in A. Chang, P. Ganz, D. Hayes, et al., (eds*). Oncology: An Evidence-Based Approach*. New York, NY: Springer-Verlag; 2006:1552–1579 Available at: http://www.cas.usf.edu/~jacobsen/Anxiety%20depression%20review.pdf (Accessed 8/12/2014).

[73] A. Greer, L. Traeger, H. Bemis, J. Solis, E. Hendriksen, and E. Park, "A Pilot randomized controlled Trial of Brief Cognitive Behavioural Therapy for Anxiety in Patients with Terminal Cancer," The Oncologist, 17, 1337-1345, 2012. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3481900/. (Accessed 26/12/2014)

[74] S. Moorey, E. Cort, M. Kapari B. Monroe, P. Hansford, K. Mannix, et al., "A cluster randomized controlled trial of cognitive behaviour therapy for common mental disorders in patients with advanced cancer," *Psychological Medicine*, 39, 713–723, 2009.

[75] D. Kissane, B. Grabsch, D. Clarke, G. Smith, A. Love, S. Bloch et al., "Supportive‐expressive group therapy for women with metastatic breast cancer: survival and psychosocial outcome from a randomized controlled trial 2," *Psychooncology*, 16, 277–286, 2007.

[76] D. Spigel, L. Butler, J. Giese-Davis, C. Koopman, E. Miller, S. DiMiceli et al., "Effects of supportive expressive group Therapy on survival of patients with metastatic breast cancer," *Cancer*, 110, 1130-1138, 2007. Available at: http://onlinelibrary.wiley.com/doi/10.1002/cncr.22890/full. (Accessed 25/12/2014)

[77] National Breast Cancer Centre and National Cancer Control Initiative, "Clinical Practice Guidelines for the psychosocial care of adults with cancer," 2003.

[78] M. Holmes, W. Chen, D. Feskanich, C. Kroenke, and G. Colditz, "Physical activity and survival after breast cancer diagnosis," *JAMA*, 25, 293:2479-86, 2005.

[79] A. Meyerhardt, E. Giovannucci, M. Holmes, A. Chan, J. Chan, G. Colditz, et al, "Physical Activity and Survival After Colorectal Cancer Diagnosis," J Clin Oncol, 1, 3527-34, 2006.

[80] C. Holick, P. Newcomb, A. Trentham-Dietz, L. Titus-Ernstoff, A. Bersch, M. Stampfer, et al, "Physical Activity and Survival after Diagnosis of Invasive Breast Cancer," *Cancer Epidemiology, Biomarkers & Prevention*, 1, 379-86, 2008.
[81] M. Irwin, A. Smith, A. McTiernan, R. Ballard-Barbash, K. Cronin, F. Gilliland, et al., "Influence of Pre- and Postdiagnosis Physical Activity on Mortality in Breast Cancer Survivors: The Health, Eating, Activity, and Lifestyle Study," *Journal of Clinical Oncology*, 20, 3958-64, 2008.
[82] Daley, H. Crank, J. Saxton,N. Mutrie, R. Coleman, and A. Roalfe et al., "Randomized trial of Exercise Therapy in Women Treated with Breast Cancer", *Journal of Clinical Oncology*, 25, 13, 2007. Available at: http://jco.ascopubs.org/content/25/13/1713.long. (Accessed 25/12/2014).
[83] Courneya, R. Segal, J. Mackey, K. Gelmon, R. Reid, C. Friedenreich, et al., "Effects of Aerobic and Resistance Exercise in Breast Cancer Patients receiving Adjuvant Chemotherapy: A Multicentre Randomized Controlled Trial," *Journal of Clinical Oncology*, 25, 4396-4404, 2007.
[84] Courneya, J. Mackey, G. Bell, L. Jones, C. Field, and A. Fairey, "Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: Cardiopulmonary and quality of life outcomes," *Journal of Clinical Oncology*, 21, 1660-1668, 2003. Available at: http://www.cebp.nl/media/m542.pdf. (Accessed 25/12/2014)
[85] P. Fobair, S. Stewart, S. Chang, C. Onofrio, P. Banks, and J. Bloom, "Body image and sexual problems in young women with breast cancer," *Psychooncology*, 15, 579-594, 2006.
[86] McNeely, K. Campbell, B. Rowe, T. Klassen, J. Mackey, K. Courneya, "Effects of Exercise on Breast Cancer Patients and Survivors; a systematic review and meta-analysis," CMAJ, 175, 34-41, 2006.
[87] V. Conn, A. Hafdahl, D. Porock, R. McDaniel, and P. Nielsen, "A meta analysis of exercise interventions among people treated for cancer," *Supportive Care in Cancer*, 14, 699-712, 2006
[88] K. Schmitz, J. Holtzman, K. Courneya, L. Masse, S. Duval, R. Kane, "Controlled physical activity trials in cancer survivors: A systematic review and meta-analysis," *Cancer Epidemiology Biomarkers & Prevention*, 14, 1588-1595, 2005. Available at: http://cebp.aacrjournals.org/content/14/7/1588.long. (Accessed 25/12/2014).
[89] A. Moadel, C. Shah, J. Wylie-Rosett, M. Harris, S. Patel, and C. Hall, et al., "Randomized controlled Trial of Yoga among a multiethnic sample of breast cancer patients: Effects on Quality of Life," *Journal of Clinical Oncology*, 25, 2007
[90] S. Culos-Reed, L. Carlson, L. Daroux, and S. Hately, "A pilot study of yoga for breast cancer survivors:Physical and psychological benefits," Psychooncology, 15, 891-897, 2006.
[91] R. Segal, R. Reid, K. Courneya, R. Sigal, G. Kenny, D. Homme, et al., "Randomized Controlled Trial of Resistance or Aerobic Exercise in Men Receiving Radiation Therapy for Prostate Cancer," Journal of Clinical Oncology, 27, 344-351, 2009.
[92] P. Windsor, K. Nicol, and J. Potter, "A randomized, controlled trial of aerobic exercise for treatment related fatigue in men receiving radical external beam radiotherapy for localized prostate carcinoma," *Cancer*, 101, 550-557, 2004.
[93] Culos-Reed SN, Robinson JL, Lau H, K. O'Connor, and M. Keats, "Benefits of a physical activity intervention for men with prostate cancer," *Journal of Sport & Exercise Psychology*, 29,118- 127, 2007
[94] B. Jereczek-Fossa, H. Marsiglia, and R. Orecchia, "Radiotherapy-related fatigue," *Critical Reviews in Oncol Hematology*, 41:317-325, 2002
[95] C. Bennett, S. Silver, B. Djulbegovic, A. Samaras, C. Blau, K. Gleason, et al., "Venous thromboembolism and mortality associated with recombinant erythropoietin and darbepoetin administration for the treatment of cancer associated anemia," *JAMA*, 299, 914-924, 2008.
[96] J. Lemieux, A. Topp, H. Chappell, M. Ennis, and P. Goodwin, "Economic analysis of psychosocial group therapy in women with metastatic breast cancer," *Breast Cancer Research and Treatment*, 100,183-190, 2006.
[97] S. Hayes, R. Spence, D. Galvão, and R. Newton, "Australian Association for Exercise and Sport Science position stand: Optimising cancer outcomes through exercise," *Journal of Science and Medicine in Sport*, 12, 428-34, 2009.
[98] Minton, A. Berger A, A. Barsevick, F. Cramp, M. Goedendorp, S. Mitchell, et al., "Cancer-related fatigue and its impact on functioning," *Cancer*, 119, 2124–30, 2013.
[99] L. Whitehead, "The measurement of fatigue in chronic illness: a systematic review of unidimensional and multidimensional fatigue measures," *J Pain Symptom Manage*, 37, 107–28, 2009.
[100] A. Aaronson, V. Mattioli, O. Minton, J. Weis, C. Johansen, S. Dalton, et al., "Beyond Treatment-Psychosocial and behavioural issues in cancer survivorship research and practice," *EJC Supplements*, 12, 54-64, 2014.
[101] W. Linden, and A. Girgis, "Psychological treatment outcomes for cancer patients: what do meta-analyses tell us about distress reduction?," *Psychooncology*, 2012;21(4):343–50
[102] K. Boyes, L. Hodgkinson, Alridge, and J. Turner, "Issues for Cancer Survivors in Australia," *Cancer Forum*, 33, 164-167, 2009.
[103] J. Bloom, R. Hoppe, P. Fobair , R. Cox, A. Varghese, D. Spiegel, "Effects of treatment on the work experiences of long-term survivors of Hodgkin's disease," *Journal of Psychosocial Oncology*, 1989, 6, 65-80. Available at: http://www.tandfonline.com/doi/abs/10.1300/J077v06n03_05?journalCode=wjpo20#.VKZFuXtrJOY. (Accessed 02/01/2015)
[104] Wingard JR, Curbow B, Baker F, Piantadosi S. Health, functional status, and employment of adult survivors of bone marrow transplantation. Ann Intern Med. 1991;114:113-118.
[105] S. Schagen, M. Muller, W. Boogerd, G. Mellenbergh, and F. van Dam, "Change in cognitive function after chemotherapy: a prospective longitudinal study in breast cancer patients," *Journal of National Cancer Institute*, 98, 1742-1745, 2006. Available at: http://jnci.oxfordjournals.org/content/98/23/1742.long. (Accessed 25/12/2014).
[106] D. Coward, "Supporting Health Promotion in Adults with Cancer," *Family & Community Health*, 19, 52S-60S, 2005.
[107] L. Forsythe, E. Kent, K. Weaver, N. Buchanan, N. Hawkins, J. Rodriguez, "Receipt of Psychosocial care among Cancer Survivors in the United States," *Journal of Clinical Oncology*, 31, 1961-69.
[108] J. Guidry , L. Aday, D. Zhang, and R. Winn, "The role of informal and formal social support networks for patients with cancer," *Cancer Practice*, 5, 241–246, 1997.
[109] A. Leis, C. Haines, and G. Pancyr, "Exploring oncologists' beliefs about psychosocial groups: implications for patient care and research," *Journal of Psychosocial Oncology*, 12, 77–87, 1994.

A. Taqaddas is a British-Pakistani and have two Bachelor of Science degrees i.e. one degree from Pakistan and from UK. She successfully completed B.Sc. with Chemistry, Botany and Zoology as her subjects of study from Pakistan. She also successfully passed B.Sc. (Hons) Therapeutic Radiography course from UK. She holds a M.Sc. Medical Physics degree from UK. She has passed Radiation Protection Supervisor Training Exam from UK in 2012.

She has experience of working as Radiotherapy Dosimetrist in UK. She works as journal reviewer (in volunteer capacity) for International Journal of Medical and Radiation Sciences Canada. She is also linked with research Wormhole, a research company registered in Canada. She is the author of first concise book on Volumetric Modulated Arc Therapy. Title of Book is Investigation of VMAT Algorithms and Dosimetry. She has experience of presenting original research papers in International Conferences such as ASTRO conference in 2013 and International conference on Radiation Medicine (ICRM 2014) in 2014. She has also acted as program chair in ICRM 2014. She has knowledge of multiple disciplines and her work has been published in the fields of Radiation Oncology, Medical/Radiation Physics, Immunology, Virology and Nano-medicine.

Miss Auj-E Taqaddas is registered with Health Professions Council UK since 2007.