

**Original Article**

**ASSOCIATION OF PATIENT RELATED RISKFACTORS WITH EFFECTIVENESS OF PALLIATIVE CHEMOTHERAPY IN CANCER PATIENTS**

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**ABSTRACT**

**Objective:** To assess the association of some risk factors on the effectiveness of palliative chemotherapy treatment in cancer patients.

**Methods:** A prospective observational study was conducted in the department of radiotherapy for a period of 6 mo. Ages, Gender, Cancer type, Physical Functioning, Anxiety and Depression, Medical Social Support, Comorbidities, Adverse Drug Reactions are defined as risk factors. The effectiveness of palliative chemotherapy treatment was defined according to Response Evaluation Criteria in Solid Tumors (RECIST). Mean and standard deviation was calculated from the age. The association between risk factors and the effectiveness of chemotherapy treatment was found by chi-square test. The level of significance was taken as  $p < 0.05$ .

**Results:** The association between risk factors and effectiveness of palliative chemotherapy treatment was found using Chi-Square test. The mean age of patients in the present study was  $50.57 \pm 12.62$  y. Females were more commonly affected. The Majority of the patients were illiterate, married and homemaker. Reproductive system related cancers (50.66%) were more predominant in the present study. A statistically significant association was observed between age ( $p=0.027$ ), physical functioning ( $p=0.0076$ ), anxiety ( $p=0.000072$ ) and depression ( $p=0.000016$ ), co-morbidities ( $p < 0.00001$ ) and adverse drug reactions ( $p < 0.00001$ ) with effectiveness of chemotherapy treatment.

**Conclusion:** By predicting these risk factors prior to the initiation of treatment, we can minimize their unfavourable effect on the effectiveness of treatment.

**Keywords:** Risk factors, Chemotherapy, Adverse drug reactions, Response evaluation criteria in solid tumours

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**INTRODUCTION**

Cancer is a complex diseases (200 different types) in which cells in a specific tissue do not completely respond to signals which regulate cellular differentiation, survival, proliferation and death, which leads to cell accumulation within the tissue, causing local damage and inflammation [1]. Roeland and Leblanc defined palliative chemotherapy as given in the non-curative setting to optimize symptom control, improve quality of life (QoL) and ideally, to improve survival [2]. These goals of the palliative chemotherapy can be met when the risk factors are monitored and when the pertinent management approaches are followed. Risk factors impede the therapeutic benefits of the therapy. Besides, they indirectly increase the disease progression in cancer patients. Therefore, our study aims to know the association of risk factors with the effectiveness of palliative chemotherapy in cancer patients.

The patient related risk factors that are studied are age, dependence of daily activities, comorbidities, anxiety and depression, social support. Barthel index was used to measure the patient's ability of performing daily activities independently and capability of patients to receive the palliative chemotherapy treatment. Patients with poor physical activity cannot withstand the chemotherapy. Comorbidities escalate the toxicity of chemotherapy treatment by physiological alteration of pharmacokinetic parameters of chemotherapy drugs. Chronic comorbidities such as heart and renal related diseases can influence the risk of febrile neutropenia which shows impact on patient's treatment outcome [3, 4]. Cumulative Illness Rating Scale (CIRS) was used to measure the burden of comorbidities. Patients with anxiety and depression lack emotional and financial support from family. As a result, their adherence to treatment regimen will be poor and it leads to treatment failure. Hospital Anxiety and Depression Scale (HADS) was used to assess the anxiety and depression in cancer patients. Social support plays an important role in cancer patients because social support has a mediating role in the effect of adaptability style. If social support can reduce the effect of life's difficulty, stress and

incidence of mood disorder, then cancer patients have improvement in chemotherapy treatment [5]. In addition, many studies indicate that more survival, better adaptability and mental health and higher quality of life are mostly seen in cancer patients receiving social support. Conversely, inadequate or unsatisfying social support leads to negative outcomes such as more stress and concern, more psychological and mental pressure and communication disorders, Poor emotional health, pessimistic attitude, hospitalization, poor survival [6, 7]. Medical Social Support Survey Scale (MSSSS) was used to measure the emotional and tangible support offered to cancer patients by their family members. The effectiveness of chemotherapy was assessed using Response Evaluation Criteria in Solid Tumors (RECIST).

The aim of the present study was to evaluate the association of Patient Related Risk factors with Effectiveness of Palliative Chemotherapy in Cancer Patients.

**MATERIALS AND METHODS**

**Study design and data collection**

This was a prospective cross sectional study conducted in the department of oncology of tertiary care teaching hospital, Kakinada for a period of 6 mo. The study was approved by Institutional ethical committee (APC/IEC/RT/18). All cancer patients of both gender, age  $\geq 18$  years, diagnosed as having cancer and receiving only palliative chemotherapy as a mode of treatment were included in the study. Cancer patients who are critically ill, receiving other treatment modalities like radiation therapy along with palliative chemotherapy and relapsed cases were excluded from the study.

**Assessment**

Patient demographics like age, gender, educational level, marital status, employment status, household composition, cancer type, type of chemotherapy, adverse drug reactions etc. were collected in a specially designed data collection form. The Barthel index scale was

used to determine the dependence of patient's daily activities and was scored as 100%-Independence, 91-99-Slight Dependence, 61-90-Moderate Dependence, 21-60-Severe Dependence, 0-20-Total Dependence. Cumulative Illness Rating Scale measures chronic medical illness burden while taking severity of the conditions into account. Hospital Anxiety and Depression Scale commonly used to determine the levels of anxiety and depression that a patient is experiencing.

The Hospital Anxiety and Depression Scale is a fourteen item scale that generates ordinal data. Seven of the items relate to anxiety and seven relate to depression. Medical Social Support Survey scale was used to assess emotional and tangible support from patient family

members. The above said scales were tabulated in a data collection form to make the final interpretation easier. Patient's response to chemotherapy for target and non-target lesions was determined by using Response Evaluation Criteria in Solid Tumors criteria. The response criteria were categorized as complete remission, partial remission, stable disease and progressive disease for both target lesions and non-target lesions.

#### Statistical analysis

Mean and standard deviation was calculated from the age. The association between risk factors and the effectiveness of chemotherapy treatment was found by chi-square test. The level of significance was taken as  $p < 0.05$

## RESULTS

**Table 1: Socio-demographic characteristics of chemotherapy patients (N=150)**

S. No.	Patient demographics	Female	Male	Total
1.	<b>Age</b>			
	15-35	16	5	21
	36-55	61	23	84
	56-75	21	21	42
	76-95	2	1	3
2.	<b>Gender</b>			
	Female	100	0	100
	Male	0	50	50
3.	<b>Cancer Type</b>			
	Reproductive System Related Cancer	74	2	76
	Digestive System Related Cancer	17	26	44
	Respiratory System	2	8	10
	Nervous System	0	2	2
	Others	7	11	18
4.	<b>Educational Level</b>			
	Less Than High School	19	3	22
	High School Graduate	23	16	39
	Associate/Bachelor's Degree	1	3	4
	Uneducated	57	28	85
5.	<b>Marital Status</b>			
	Married	75	48	123
	Widowed	23	2	25
	Unmarried	1	1	2
6.	<b>Employment Status</b>			
	Full Time Job	20	37	57
	Unemployed	0	12	12
	Homemaker	81	0	81
7.	<b>Household Composition</b>			
	Lives With Partner	5	2	7
	Lives Alone	0	0	0
	Lives With Partner, Spouse Or Children	70	46	116
	Lives With Children	21	1	22
	Lives With Family Members	3	2	5

The mean age of patients in the present study  $50.57 \pm 12.62$  y. Females were more commonly affected. The Majority of the patients were illiterate, married and homemaker. Reproductive system

related cancers (50.66%) were more predominant in the present study. In the reproductive system related cancers, breast cancer was found to be more common (33.3%).

**Table 2: Daily activities of chemotherapy patients based on barthel index**

S. No.	Scoring	Female	Male	Total
1.	100-Independence	63	30	93
2.	91-99-Slight Dependence	8	5	13
3.	61-90-Moderate Dependence	25	14	39
4.	21-60-Severe Dependence	3	2	5
5.	0-20-Total Dependence	0	0	0
6.	Total	99	51	150

The majority of the patients were independent (62%) and can perform their daily activities on their own. A patient having a Barthel index score of 100 was considered as independent. So we can predict that patients were likely to be discharged to

community living, i.e. Independent in transfers and able to walk or use wheelchair independently. Patients with score 100 i.e. independent were considered to be capable of receiving chemotherapy treatment

Table 3: Co-morbidities of cancer patients based on cumulative illness rating scale

S. No.	Co-Morbidities	Female	Male	Total
1.	Hypertension	1	1	2
2.	Hypertension On Medication	12	5	17
3.	Diabetes Mellitus	0	1	1
4.	Diabetes Mellitus On Medication	2	0	2
5.	Surgery	13	1	14
6.	Head and Neck	7	15	22
7.	Liver Disease/Jaundice/Gall Stones	2	1	3

Table 4: Anxiety and depression of chemotherapy patients

S. No.	Hospital anxiety and depression scale	Female	Male	Total
1.	<b>Anxiety</b>			
2.	Normal	83	42	125
3.	Borderline abnormal	1	3	4
4.	Abnormal	15	6	21
5.	<b>Depression</b>			
6.	Normal	80	40	120
7.	Borderline Abnormal	3	3	6
8.	Abnormal	16	8	24

Table 5: Emotional and tangible support to chemotherapy patients

S. No.	Medical social support survey scale	Female	Male	Total
1.	100.00%	2	0	2
2.	81.20%	85	45	130
3.	79.60%	0	1	1
4.	64.00%	2	2	4
5.	62.23%	2	0	2
6.	57.81%	0	2	2
7.	40.62%	6	2	8
8.	29.68%	1	0	1

Table 6: Effectiveness of chemotherapy treatment (RECIST Criteria)

S. No.	RECIST criteria	Female	Male	Total
1.	Complete Remission	0	0	0
2.	Partial Remission	26	14	40
3.	Stable Disease	34	20	54
4.	Progressive Disease	37	19	56

Table 7: Association between risk factors and effectiveness of chemotherapy treatment

S. No.	Risk factors	RECIST criteria			Statistic	P-Value
		PR	SD	PD		
1	<b>Age (In Years)</b>					
	15-35	4	6	10	$\chi^2=$ 14.2241	p = <b>0.027231*</b>
	36-55	28	28	26		
	56-75	5	19	21		
76-95	0	0	3			
2	<b>Gender</b>				$\chi^2=$ 0.0724	p = 0.964467
	Female	26	34	40		
4	<b>Barthel Index</b>				$\chi^2=$ 17.472	p = <b>0.007694*</b>
	Independence	29	33	27		
	Slight Dependence	2	8	3		
	Moderate Dependence	9	11	20		
5	<b>Severe Dependence</b>	0	1	7	$\chi^2=$ 41.6832	p <b>&lt;0.00001*</b>
	<b>Co morbidities</b>					
	Hypertension and HTN on Medication	13	4	2		
	Diabetes Mellitus and DM on Medication	0	1	2		
	Surgery	13	0	1		
6	Head and Neck	7	15	0	$\chi^2=$ 24.2136	p = <b>0.000072*</b>
	Liver Disease/Jaundice/Gall Stones	1	0	2		
	<b>Anxiety</b>					
	Normal	38	48	39		
	Borderline abnormal	2	1	1		
	Abnormal	0	3	18		

7	<b>Depression</b>					
	Normal	37	46	35	$\chi^2=$	$p =$
	Borderline Abnormal	0	2	4	27.4174	<b>0.000016*</b>
	Abnormal	0	5	21		
8	<b>Medical Social Support Survey</b>					
	100.00%	1	0	1	$\chi^2=$	$p =$
	81.20%	34	46	52	0.9409	0.918619
	79.60%	0	1	0		
	64.00%	1	1	2		
	62.23%	0	1	0		
	57.81%	1	1	0		
	40.62%	2	2	3		
	29.68%	1	0	0		

[PR= Partial remission, SD= Stable disease, PD= Progressive disease, \*p value<0.05 was statistically significant].

## DISCUSSION

Statistically significant relationship was observed between age ( $p=0.027$ ), physical functioning ( $p=0.0076$ ), anxiety ( $p=0.000072$ ) and depression ( $p=0.000016$ ), co-morbidities ( $p<0.00001$ ) and adverse drug reactions ( $p<0.00001$ ).

Usually age of the cancer patient has an inverse relationship with the effectiveness of chemotherapy treatment. As the age of the patient increases, the physiological functioning decreases, this in turn affects the pharmacokinetic pattern of drugs and thus pharmacodynamics too. The tolerance to side effects to drugs will also decrease which in turn increases the frequency of adverse drug reactions. Indeed, this intolerance due to adverse drug reactions will delay the treatment, dose adjustments and sometimes cessation of treatment. Eventually, this leads to progression of disease.

Physical functioning was found to be a risk factor for effectiveness of chemotherapy treatment because, age, gender, chronic health conditions (co-morbidity), stage of cancer, site of cancer changes the physical functioning of cancer patient which leads to delay in chemotherapy treatment. Chronic health conditions, depressive symptomatology moderate the effect of intervention on physical function [8].

Co-morbidity is defined as the "coexistence of disorders in addition to a primary disease of interest. The extent to which co-morbidity affects how well treatments are tolerated will necessarily relate to the type and severity of co-morbidity and the specific treatment. For example, patients with severe chronic airways disease are unlikely to tolerate pneumonectomy for lung cancer, but may tolerate treatment that does not affect the lung and patients with severe renal impairment are unlikely to tolerate nephrotoxic chemotherapy but may tolerate other chemotherapy drugs. Several authors have reported that co-morbidity does not increase the frequency or severity of treatment complications in some circumstances [9, 10]. In contrast, other studies have reported higher rates of complications among cancer patients with co-morbidity [11, 12]. An important factor that impacts on the cancer treatment uptake and completion is interaction with other drugs. Those with co-morbidity are likely to be on several prescribed, over-the-counter, or alternative medications, which can interact with each other and with chemotherapeutic agents, potentially leading to increased toxicity, reduction in the effectiveness of a therapeutic regime, or reduction in compliance [13, 14].

The occurrence of anxiety and depression worsen the cancer condition which leads to delay in treatment outcome. In an experimental study, there is evidence that psychological stress (anxiety and depression) can affect a tumour's ability to grow and spread. This psychological stress is associated with higher rates of death, although the mechanism for this outcome is unclear. It may be that people who feel helpless or hopeless do not seek treatment when they become ill, give up prematurely or fail to adhere to potentially helpful therapy, engage in risky behaviours such as drug use, or do not maintain a healthy lifestyle, resulting in premature death. So, due to increased growth and spread of tumour and fail to adhere to potentially helpful therapy, there will be delayed treatment outcome [15]. Planned teaching programme will be

effective in improving knowledge of patients about the effect of risk factors. The importance of planned teaching programme was reported in a study [16]. Apart from these factors, lifestyle and diet *al.* so plays an important role in effectiveness of therapy. It was reported that smokers and non-vegetarians are more prone to oral cancer [17].

## CONCLUSION

Usually age of the cancer patient has an inverse relationship with the effectiveness of chemotherapy treatment. As the age of the patient increases, the physiological functioning decreases, this in turn affects the pharmacokinetic pattern of drugs and thus pharmacodynamics too. However, age as a risk factor cannot be managed. Physical functioning has an impact on treatment outcome. If the physical functioning deteriorates, then the treatment was stopped till the physical functioning regains to tolerate the treatment which leads to delay in chemotherapy treatment and show impact on treatment outcome. Physical functioning can be assessed using Karnofsky performance status scale, Eastern Cooperative Oncology Group scale, Barthel index. The effect of comorbidity on the effectiveness of chemotherapy depends on the type and severity of comorbidity. There is a dilemma regarding the effect of comorbidity on the overall survival and its effect on the treatment outcome. Anxiety and depression itself worsens the cancer condition by affecting the tumors ability to grow and spread. Adverse drug reactions are inevitable. They result in dose alterations or temporary cessation of the treatment, which altogether results in disease progression. In the present study, statistically significant association between age, physical functioning, co-morbidities, anxiety and depression and effectiveness of chemotherapy treatment was observed. So, by predicting these risk factors prior to the initiation of treatment, we can minimize their unfavourable effect on the effectiveness of treatment.

## AUTHOR CONTRIBUTION

Vinodkumar Mugada-concept, design, literature search, manuscript preparation, editing and review

Pidaparthi Prashanth-concept, design, definition of intellectual content

Polaramsetti Snehapriyanka-concept, data acquisition, data analysis, statistical analysis

Pedasanaganti Jyothirmai-data acquisition, data analysis, statistical analysis

## LIMITATION

The sample size was relatively small due to short duration of the study. Similar studies with good sample size are required to draw a proper conclusion.

## ABBREVIATION

CIRS-Cumulative Illness Rating Scale, HADS-Hospital Anxiety and Depression Scale, MSSSS-Medical Social Support Survey Scale, RECIST-Response Evaluation Criteria In Solid Tumours.

**CONFLICTS OF INTERESTS**

All authors have none to declare

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