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ASSESSMENT OF MEDICATION ADHERENCE AND FACTORS INFLUENCING NONADHERENCE AMONG CANCER PATIENTS CHEMOTHERAPY–AN OBSERVATIONAL PROSPECTIVE STUDY

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ABSTRACT

According to World Health Organization, Cancer is the uncontrolled growth of cells, which can invade and spread to distant sites of the body. Cancer can lead to severe health consequences and conditions possibly leading to death. In cancer patients, poor adherence to medication may lead to medical complications, more frequent doctor visits and longer hospitalizations. This hospital based case study was undertaken with the objective of determining barriers of medication adherence in patients receiving chemotherapy, determining the type of cancer showing less adherence rates among the prescribed chemotherapy regimens, and to determine the regimen to which patients showed the least adherence rates. Out of the 174 patients studied, 75.8% were found to be adherent and 24.1% to be non-adherent to the prescribed chemotherapy. Majority of patients were diagnosed with breast cancer (15.51%), head and neck cancer (14.9%) and ovarian cancer (13.21%). Of the prescription sheets reviewed,20.6% were prescribed with Taxol (175mg/m^2 IV) and Carbo 5 AUC (maximum dose 800mg/body) regimen and 19.5% were receiving cisplatinalone (50 mg in 1pint normal saline given IV for half hour).Among the various regimens prescribed AC (Adriamycin 60mg/m^2 and Cyclophosphamide 600mg/m^2) regimen (21.4%) has shown more non adherence levels. Among the total number of non-adherence cases, 50% was due to patient related factors. The other barriers for adherence among patients included economic factors (23.8%) followed by social factors(9.5%), drug related(14.2%) and the least non adherence was seen due to disease related factors(2.3%). From the present study it was concluded that patient related factors significantly affect the adherence levels. It was observed that most of the patients miss or delay their chemotherapy cycle due to lack of convenience and forgetfulness of attending the chemotherapy cycle appointments according to the date prescribed by the oncologist, and also due to lack of knowledge about the benefits and risks associated in receiving chemotherapy. This study reassures the role of adherence with treatment regimens in patient survival and better quality of life.

KEYWORDS: *Adherence, cancer, chemotherapy, patient*

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INTRODUCTION

According to World Health Organization, cancer is the uncontrolled growth of cells which can invade and spread to distant sites of the body. It can have severe health consequences and conditions leading to death.[1]Over the last four decades, the incidence of cancer rise phenomenally. In spite of advancements in medical and diagnostic sciences, the health standard and general well-being of patients with tumour remains inferior.[2]The clinicians therefore focus on improving the quality of life of the cancer patients rather than curing, as the curing process seems to deteriorate the quality of life and cure is not certain. It has been found that more than 30% of cancer deaths are preventable on avoiding risk factors with lifestyle modifications, early detection, accurate diagnosis, and effective treatment as these measures can alleviate pain and improve survival rates. Treatment options include chemotherapy, radiotherapy and surgery; the treatment to be given is determined based on the tumour stage, type of cancer and available resources.[3] Despite advanced treatments in oncology, medication non adherence is a cause of concern. WHO defines Medication adherence to long-term therapy as "the extent to which a person's behaviour (in terms of taking medication, following diets, or executing lifestyle changes) coincides with healthcare advice.''[4] In cancer patients, poor adherence may be associated with disease progression and resistance to medication. It can lead to medical complications, more frequent doctor visits and more frequent and longer hospitalizations. Even some participants in clinical trials are non-adherent, which can lead to inaccurate information about medication safety and efficacy.[5]Therefore, a critical component to the success of these medically prescribed cancer therapies (e.g. chemotherapy or radiation) is patient adherence.[6] Non-adherence to medication regimen may affect the patient's health by causing further complications. Non-adherence is said to be intentional when the patient decides not to take the prescribed medication, often due to adverse side effects or when the treatment outcomes are not clear, poor or take a long time. Unintentional adherence may result from forgetting to take the medication or misunderstanding the instruction.[7] Involving cancer patients in all aspects of decision making process has been shown to increase their motivation and adherence thereby making the role of physicians more important in improving patient adherence. It requires patient-physician ongoing communication, including patient education, developing tailored treatment regimen, regularly scheduled meeting, adherence monitoring and follow up to evaluate patient's responses to therapy which may help to identify adherence issues and the resulting effect on outcomes. It also requires clinicians to listen to the patient's needs, concerns, complaints, preferences and wishes. Poor communication between the patient and the physician with regards to the medication regimen, side effects and new possible treatments, particularly complex regimens with new side effects, may also explain the patient's high non-adherence.[8]In the current scenario, intervals of chemotherapy cycles are not being followed as recommended by the prescriber. Non adherence to the recommended intervals between each cycle of chemotherapy may lead to drug resistance, disease progression, recurrence of the disease and even increase risk of mortality.[9]The various barriers influencing adherence in patients receiving chemotherapy should be identified and brought to the notice of the prescriber and health care staff in order to improve the adherence of the patient to the chemotherapy regimen.

The possible factors influencing adherence in patients receiving chemotherapy are listed below in detail:

- Economic factors: including poor family background or no insurance scheme.
- Social factors: including lack of family support and social support.
- Drug related factors: including adverse drug reactions, other consequences such as pain, alopecia, nausea, vomiting and diarrhoea.
- Disease related: including comorbidities, severity of the disease, long term therapy, and physical weakness.
- Patient related: including lack of knowledge, negligence, fear, forgetfulness, or lack of traveling facility.
- Prescriber related: including lack of patient counselling, lack of time and negligence.

In our present study we have determined barriers of medication adherence among cancer patients receiving chemotherapy using a medication adherence questionnaire (MAQ) which explores both patient's medication taking behaviour and barriers to adherence. We have also determined the particular cancer condition in which non-adherence is mostly seen and also the most common regimen with less adherence rate.

MATERIALS AND METHODS

The study was conducted at a super speciality cancer care centre.This was a prospective observational study. The study was carried out from September 1st 2016 to February 1st 2017.The study was approved by Sarada Vilas College of Pharmacy institutional ethics committee on human subject research and ethical clearance certificate was issued on 22/08/16.

Inclusion criteria

1. Patients receiving chemotherapy or who have received chemotherapy.
2. Patients who have received at least one cycle of chemotherapy
3. Patient of all age groups

Exclusion criteria

1. Patients who are not admitted or not receiving chemotherapy at day-care.
2. Patients who are not ready to cooperate to the study conducted.
3. Patients who expired during the study.

Sources of data

Patient case records, Patient or patient's caretaker(s) interview, Treatment chart.

Method

Preparation of data collection form

A specially designed data collection form (Annexure III) was devised for the study it included demographic details like patient's name, age,gender, family history, social habits and clinical data such as diagnosis, past medication history, comorbidities, stage of cancer. It also included details regarding the drug, dose, frequency, duration of administration, pre medication and post medication of chemotherapy was also included. The same details were documented electronically in specially designed database (Google forms).

Patient enrolment

Patients fulfilling the study criteria were enrolled into the study after obtaining their consent.Patients were enrolled from in-patients general wards, private wards and day-care centres.

Data collection

All relevant details of the enrolled patients were obtained from various data sources and documented in the data collection form.

Assessment of adherence to chemotherapy in the hospital[10]

The adherence among patients receiving chemotherapy was assessed using a validated medication adherence questionnaire (MAQ), which explores both patient's medication taking behaviour and barriers to adherence.The items included in the questionnaire were categorized based on economic factors, social factors, drug related factors,disease related factors, patient related and even prescriber related factors. The enrolled patients were reviewed on the basis of chemotherapy regimen prescribed and the cancer diagnosed.

RESULTS

Table 1
TYPES OF CANCER

TYPE OF CANCER	FREQUENCY	PERCENTAGE
BREAST	27	15.5%
HEAD AND NECK	26	14.94%
OVARIAN CANCER	23	13.21%
LYMPHOMA	14	8.04%
STOMACH	13	7.47%
CERVICAL	13	7.47%
LUNG	13	7.47%
OESOPHAGUS	12	6.87%
COLON	6	3.44%
RECTAL	5	2.87%
MULTIPLE MYELOMA	4	2.2%
PANCREATIC NEUROENDOCRINE	3	1.72%
RECURRENT MEDULLABLASTOMA	2	1.14%
UTERUS	2	1.14%
TESTICULAR	2	1.14%
BLADDER	2	1.14%
ADENOCARCINOMA	2	1.14%
SQUAMOUS CELL CARCINOMA	1	0.57%
OSTEOSARCOMA	1	0.57%
PROSTATE	1	0.57%
TOTAL	174	100%

Out of the total number of cancer patients, it was found that 15.5 % (n=27) patients had breast cancer and 14.9 % (n=26) patients had head and neck cancer. Details of the types of cancer are described in table 1.

TABLE 2
NUMBER OF CYCLES COMPLETED

NO.OF CYCLES COMPLETED	FREQUENCY	PERCENT
ONE	**2**	**.12%**
TWO	**51**	**29.3%**
THREE	**56**	**32.2%**
FOUR	**39**	**22.4%**
FIVE	**13**	**7.5%**
SIX	**13**	**7.5%**
TOTAL	**174**	**100.0%**

The number of cycles completed by the patient in the study period was found. Out of the 174 patients, 32.2% (n=56) had completed three cycles, 29.3% (n=51) had completed two cycles, 22.4% (n=39) had completed four cycles and 7.5 %(n=13) had completed five and six cycles [table 2].

Table 3
MONOTHERAPY

Regimen	Frequency	percent	adherent cases	non-adherent cases
Cisplatin	34	19.5%	26	8
Bortezomib	4	2.4%	4	0
5FU+Leucoverin	8	4.6%	8	0
Liposomal doxorubicin	1	.6%	1	0
Paclitaxel	6	3.4%	4	2
Methotrexate	1	.6%	1	0
Bendamustine	1	.6%	1	0
Docetaxel	1	.6%	0	1
Gemcitabine	1	.6%	1	0
Taxol	1	.6%	1	0
Total	58	33.5%	47	11

In the treatment regimen prescribed 33.5 %(n=58) were administered mono drug therapy. Cisplatin was the most prescribed regimen with 19.5 %(n=34) receiving it, followed by 5FU (5 Fluorouracil) +Leucoverin with 4.6 %(n=8), and paclitaxel regimen with 3.4 % (n=6)[table 3].

TABLE 4
MULTIDRUG THERAPY

Regimen	Frequency	Percent	adherent cases	non-adherent cases
Cyclophosphamide/vincristine	2	1.1%	2	0
PEM and CARBO regimen	5	2.9%	3	2
GEM and CARBO regimen	5	2.9%	3	2
AC regimen	16	9.2%	7	9
Taxol and Carbo regimen	36	20.7%	32	4
EOX regimen	1	.6%	0	1
FOLFOX regimen	3	1.7%	1	2
DCF regimen	5	2.9%	4	1
ECF regimen	13	7.5%	10	3
ICE regimen	2	1.1%	1	1
ABVD regimen	2	1.1%	2	0
CAPOX regimen	2	1.1%	2	0
CYCLO and CARBO	1	.6%	1	0
VAC regimen	3	1.7%	2	1
R-CHOP regimen	2	1.1%	2	0
EP and PE regimen	3	1.7%	1	2
GEM and CISPLATIN	2	1.1%	1	1
Inj.Adriamycin/Paclitaxel	1	.6%	1	0
PEM and Cisplatin regimen	1	.6%	1	0
Ifosfamide and Carboplatin	1	.6%	1	0
Doxorubicin and oxaliplatin	1	.6%	1	0
PEB regimen	1	.6%	1	0
Cisplatin and 5FU	4	2.3%	3	1
TOTAL	116	66.1%	85	31

In the study, most of the prescriptionswere multidrug therapy combinations like Taxol and Carbo with the highest percentage of 20.7 %(n=36) followed by AC regimen 9.2 %(n=16), ECF(Epirubicin,Cisplatin, Fluorouracil) regimen 7.5 %(n=13)[table 4].

In our study it was found that AC regimen(21.4%) has more non adherence levels because it reduces the number of WBC in the blood(neutropenia), increasing the risk of infections. Likewise, neutropenia and leucopoenia are identified as the most commonly reported adverse drug reaction among patients receiving chemotherapy. Most of the chemo drugs, such as cisplatin, carboplatin, 5-flurouracil, epirubicin and cyclophosphamide are likely to cause alopecia, nausea vomiting and diarrhoea. It was observed that 14.2% of patients were non adherent to chemotherapy prescribed due the adverse drug reactions experienced. We found that the resistance to anti emetics or higher sensitivity to chemotherapy regimen caused the patient to suffer more and eventually deteriorated their quality of life, consequently causing non adherence.

Table 5
ADHERENCE VS. NON-ADHERENCE

Have you missed any chemotherapy cycle since beginning?	FREQUENCY	PERCENT
NO	132	75.9%
YES	42	24.1%
TOTAL	174	100.0%

Out of the 174 cases reviewed, it was found that 75.9% (n=132) were adherent to the chemotherapy prescribed and 24.1% (n=42) were non-adherent. In our study it was seen that majority of the patients had high adherence to the chemotherapy and very few patients showed less adherence level. The study analysed an increased compliance to chemotherapy due to good interaction between patient and health care team of the hospital. Details described on above table [table 5].

Table 6
ADHERENCE ON THE BASIS OF CO-MORBIDITIES

			HAVE YOU MISSED ANY CHEMOTHERAPY CYCLE SINCE BEGINING?		
			NO	YES	
CO-MORBIDITIES	YES	COUNT	27	8	35
		%WITHIN CO-MORBIDITIES	77.1%	22.9%	100.0%
	NO	COUNT	104	34	138
		%WITHIN CO-MORBIDITIES	75.4%	24.6%	100.0%
TOTAL		COUNT	131	42	173
		%WITHIN CO-MORBIDITIES	75.7%	24.3%	100.0%

From the assessment of adherence based on the presence of co morbidities it was found that 71.7% (n=27) with co morbid condition were adherent to the chemotherapy and 22.9% (n=8) of the patients were non-adherent to the chemotherapy. Similarly, 75.4% (n=104) with no co morbidities were adherent to the prescribed chemotherapy and 24.6% (n=34) were not adherent[table 6].

Table 7
CHI-SQUARE TESTS

	VALUE	Df	Asymp.Sig.
Pearson chi-Square	**.048**	**1**	**.826**

Table 8
ASSESMENT OF ADHERENCE BASED ON STAGE OF CANCER

		HAVE YOU MISSED ANY CHEMOTHERAPY CYCLE SINCE BEGINNING?		
		NO	YES	Total
stage_ca1	Stage 4	25	8	33
	Count	75.8%	24.2%	100.0%
	% within stage_ ca1			
	Stage 1-3	51	8	
	Count	86.4%	13.6%	59
	% within stage_ ca1			100.0%
Total	Count	76	16	92
	% within stage_ ca1	82.6%	17.4%	100.0%

In our study it was found that 75.8% (n=24) of the study population with stage 4 cancer and 86.4% (n=51) with stages 1-3 cancer were non-adherent to the prescribed chemotherapy. Similarly, 24.2% (n=8) of the study population with stage 4 cancer and 13.6% (n=8) with stage 1-3 cancer were adherent to chemotherapy. A total 82.6% (n=76) did not adhere to their treatment and 17.4% (n=16) were adherent[table 8].

Table 9
Chi-Square Tests

	Value	Df	Asymp.Sig. (2-sided)
Pearson Chi-Square	1.681	1	.195

Table 10
Cycles category * HAVE YOU MISSED ANY CHEMOTHERAPY CYCLE SINCE BEGINNING? Cross tabulation

			Total
Cycles category	>=4 cycles	Count	65
		% within Cycles category	100.0%
	1-3 cycle	Count	108
		% within Cycles category	100.0%
Total		Count	173
		% within Cycles category	100.0%

In our study population, majority of patients n=108 were receiving or had received 1-3 cycles of chemotherapy and n=65 patients were receiving or had received 4 cycles or more. The total numbers of patients were found to be 173 [table 10].

Table 11
Chi-Square Tests

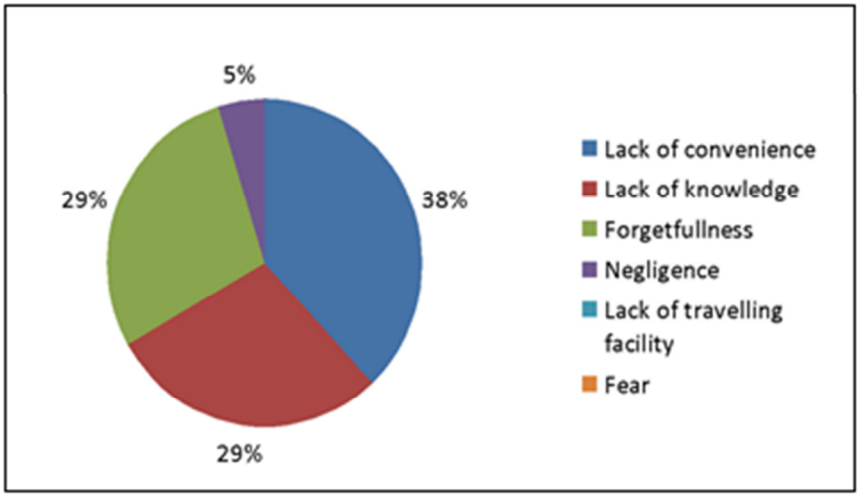
	Value	Df	Asymp.Sig. (2-sided)
Pearson Chi-Square	5.186	1	.023

Table 12
FACTORS INFLUENCING ADHERENCE

Factors influencing adherence	No. Of non-adherent cases (n=42)	Percent
Patient related	21	50%
Economic	10	24%
Social	4	10%
Drug related	6	14%
Disease related	1	2%
Prescriber related	0	0%
TOTAL	42	100%

Among the factors influencing adherence, patient related factors were 50%(n=21),Economic factors were 24%(n=10),drug related factors were 14%(n=6),Social related factors were 10%(n=4) and disease related factors were 2%(n=1). It was found that prescriber related factors did not influence the adherence of the patient [table 12].

Graph 1
PATIENT RELATED FACTORS AFFECTING ADHERENCE



The major patient related factor affecting adherence was lack of convenience accounting 38%.Forgetfulness and lack of knowledge were the second most common factors accounting 29% of the total cases, followed by negligence which was seen in 5% of the study population [graph 1].

Table 13
ECONOMIC RELATED FACTORS

Economic factors	No. of non-adherent cases
Poor family background	10
No insurance	0

Out of the total 42 non-adherent cases, 10 patients were non-adherent due to economic related factors. The major economic factor was found to be poor family background accounting 100% (n=10) Insurance factor (n=0) did not play any role in the adherence levels among the patients [table 13].

CONCLUSION

From the present study it is concluded that patient related factors have a greater impact on the adherence levels among patients receiving chemotherapy. The three main barriers related to patient adherence were found to be lack of convenience, lack of knowledge and forgetfulness. The other factors such as economic, social, drug and disease related also influenced the adherence levels of patients. Breast cancer patients mostly reported non adherence followed by head and neck cancer, and ovarian cancer patients. As demonstrated in this study, lower adherence levels with chemotherapy regimen was mostly seen among patients prescribed with AC regimen. The study concluded that there is a positive impact of pharmacist initiated patient counselling on adherence to medication therapy in patients receiving chemotherapy. This study reaffirms the role of adherence to treatment regimens in patient survival and better quality of life.

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CONFLICT OF INTEREST

Conflict of interest declared none.

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