FATIGUE IN EARLY STAGE AMONG JORDANIAN PATIENTS WITH CANCER RECEIVING CHEMOTHERAPY

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Abstract

The purposes of this study were to (1) examine the impact of Chemotherapy on fatigue in Jordanian cancer patients, and (2) to chemotherapy related fatigue (CRF) with selected demographic variables such as age, sex, marital status, income, level of education, type of cancer, stage of disease , type of chemotherapy, body mass index, smoking and hemoglobin level. One group quasi-experimental co-relational design was used with 43 patients who had been diagnosed with cancer and required Chemotherapy treatment. Fatigue was measured using Piper Fatigue Scale (PFS). Data was collected over a period of six months and analyzed using descriptive statistics, paired-sample t-test, and Pearson Product Moment Correlation. Statistically significant differences were found between total fatigue scores as well as on behavioral, affective, sensory, and cognitive dimensions of PFS, before starting chemotherapy treatment and after 4 weeks from receiving the first dose of chemotherapy treatment.

Key words: **Jordan, cancer patients, fatigue, chemotherapy**

1. Introduction

Fatigue is one of the most prevalent symptoms of patients with cancer (1). It occurs across all ages, genders, cancer diagnoses, stages of disease, and treatment regimens (2). Cancer Related Fatigue (CRF) is different from everyday tiredness, which can be reversed by rest or sleep. It is characterized by an overall lack of energy, cognitive impairment, somnolence, mood disturbance, or muscle weakness (The National Comprehensive Cancer Network (NCCN), 2013). It is a multidimensional phenomenon, which evolves over time, compromising physical energy, mental capacity and the psychological condition of the patient with cancer (3).

Studies showed that 82-96% of patients receiving chemotherapy or radiotherapy (4, 5) suffer from fatigue during their treatment. And in the same magnitude; patients with metastatic disease suffered from fatigue (6). CRF is under reported and is under-evaluated by health care givers (7) despite the presence of growing evidence on the impact of CRF on quality of life (QoL) (8).

Cancer Related Fatigue can be caused or potentially predisposed by various factors. A multidimensional model which includes situational, biological, physical symptoms and psychological symptoms, has been explored for CRF, beside that situational dimensions; inpatient status, analgesic use and stage of cancer were also correlated significantly with fatigue level (9). For a biological dimension hemoglobin level was an independent predictive factor for CRF ($P = 0.02$) (9). The impact of anemia on CRF may be different depending on onset time, patient age, and co-morbidity (10).

Despite the high prevalence of fatigue and potential negative effect on patients' activities and emotional

well-being, research in fatigue is still underdeveloped and there are no studies reporting on CRF among Jordanian population. So, this study is an attempt to explore fatigue among Jordanian cancer patients who are being treated with chemotherapy in Jordan. In addition, it is anticipated that this study will have the potential to motivate staff to take fatigue into consideration while providing care for oncology patients.

Methods

Design

One group quasi-experimental correlational design was used to examine the impact of chemotherapy treatment on Jordanian cancer patients' fatigue, and to examine the relationship between selected demographic variables and fatigue.

Sample

A consecutive sampling procedure was used to recruit potential participants for this study. The inclusion criteria are as follows: (a) 18-65 years old, (b) has no history of psychiatric or mental problem, (c) has chemotherapy for the first time, (d) is treated with chemotherapy only, (e) has Hemoglobin (Hb) level above 12 g /dl at the beginning of the study, (g) has no history of cardiac, respiratory or medical illnesses, (h) is able to give verbal consent to participate in this study, and (i) diagnosed with solid and metastatic disease.

The sample size was determined by Cohen (1988) formula. Cohen identified three levels for the effect of the sample size when using Paired Sample T test: small 0.2, medium 0.5, and large 0.8. Based on this classification and literature review, the medium effect size for comparison between two means was anticipated for this study. Testing one tailed hypothesis at significant level of alpha 0.05, the sample size was determined to be 43 participants. Therefore, the convenience sample of 43 participants who were treated with chemotherapy at KHCC, and met the inclusion criteria, agreed to participate, and were able to complete the study measurements participated in this study. The researcher interviewed each participant using the designated questionnaires PFS and DDS of the study, twice, immediately before receiving first cycle of chemotherapy and after 4 weeks from receiving first dose of chemotherapy treatment.

Setting

The King Hussein Cancer Center (KHCC) is a medical center located in Amman City, the capital of Jordan. It treats both adult and pediatric patients. KHCC treats over 3500 new cancer patients each year from Jordan and the region. KHCC has established programs that focus on all stages of comprehensive cancer care: from prevention and early detection, through diagnosis and treatment, to palliative care.

Instrumentation

The following instruments were used to collect data from all participants in this study:

1. Demographic Data Sheet

The Demographic Data Sheet (DDS) was developed by the researcher to elicit background information about the patients. The DDS includes questions related to age, marital status, gender, level of education, monthly income, occupation, religion, type of cancer, stage of disease, complications of cancer, type of chemotherapy y, dose of chemotherapy, chemotherapy side effects, body mass index, hemoglobin level at the beginning of treatment, hemoglobin level after 4 weeks from receiving first dose of chemotherapy treatment

2. Piper Fatigue Scale (PFS)

The Piper Fatigue Scale (PFS) is a multidimensional tool designed to measure the level of fatigue subjectively, and has been widely used in research. It has the potential to differentiate three levels of fatigue; mild, moderate and severe (11). Piper Fatigue Scale (PFS) is congruent with the conceptual framework of this study, which acknowledges fatigue as a subjective phenomenon.

After gaining permission from the original author, the instrument was translated to Arabic to minimize barriers of assessment with Arabic participants. The translated version of the instrument was back translated to ensure content and semantic validity. Content validity was assessed by a panel of experts in nursing who reviewed the items for clarity, relevance, comprehensiveness, understandability, and ease of administration. The panel of experts recommended no modifications.

Before embarking on the full study, a pilot test of the Arabic version was conducted with 10 participants within the target population to ensure that the tool is readable and can be understood by those who will use it. The pilot study indicated that Arabic version of PFS was in general readable, and easily understood. Participants did not request any additional information to be included in the questions. Structured interview for each participant required from 10 to 15 minutes. Reliability coefficient alpha was calculated for total PFS scores and subscales scores. The results showed that the Arabic version of PFS is a reliable instrument, with internal consistency of the entire Arabic version of PFS (alpha =0.947), and for the four subscales: behavioral, affective, sensory, and cognitive dimension (alpha = 0.915, 0.807, 0.952, and 0.864) respectively.

Ethical consideration

The study protocol was approved by the Institutional Review Board at King Hussein Cancer Centre administration, to conduct the study. Daily visits were made to the setting to check for participants who met the inclusion criteria. Once a participant was identified, verbal consent was obtained after providing adequate information about the significance and purposes of the

study. Participants were assured that participation was voluntary, and participants were told to feel free to withdraw at any time. Participants were assured that their responses would be treated confidentially and information that might reveal their identity would not be recorded and only aggregated data would be communicated.

Results

Participants' Characteristics

All participants were treated with different types of chemotherapy at KHCC. The age of participants ranged from 21-73 years (M= 45.98, SD= 13.27). Most participants were female (n=26), married (n= 36), had high school diploma (n=30), and were employed (n=23); 23 participants had a monthly income less than 650 JD, about 93% were non-smokers, diagnosed with breast cancer (n=17), obesity was present in about 64.4% of participants, most of them were treated with Anthracyclin based regimen. (See Table 1 (Part A below, Part B, top of page 9), for sociodemographic characteristics of the sample).

Table 1: Sociodemographic Characteristics of the Sample (Part A. Part B next page)

Character	Category	Frequency	%	Mean	Standard deviation	Range
Sex	Male	17	39.5			
	Female	26	60.5			
Age	<50	27	62.7	45.98	13.27	21-74
	50-59	10	23.3			
	>60	6	14			
Marital Status	Single	6	14			
	Married	36	83.7			
	Widow	0	0			
	Divorced	1	2.3			
Level of Education	Illiterate	0	0			
	≤ High School	13	30.2			
	>High School	30	69.8			
Occupation	Unemployed	20	46.6			
	Employed	23	53.4			
Monthly Income (JD)	≤650	23	53.4			
	>650	20	46.6			
Smoking	Non	29	67.4			
	Ex-smoker	11	25.6			
	Smoker	3	7			
Duration Time to reach the hospital	≤1hour	34	79			
	.>1hour	9	21			
Type of Transportation	Own car	39	90.7			
	Public	4	9.3			
	Others	0	0			
Chemotherapy Dose Number	1	35	81.4			
	2	3	7			
	3	3	7			
	4	2	4.7			
Type of Cancer	Breast	17	39.6			
	Bladder	1	2.3			
	Colon	5	11.6			
	Lymphoma	8	18.6			
	MM	1	2.3			
	NSCLC	4	9.3			
	Ovarian	1	2.3			
	Prostate	3	7			
	Stomach	1	2.3			
	Testicular	2	4.7			

Table 1: Sociodemographic Characteristics of the Sample (Part B)

Type of Chemotherapy	Anthracyclin based regimen: AC+ FEC+ doxorubicin.	20	46.5			
	Platinum based regimen: FOLFOX, DCF (Cisplatin+Docetaxel+Flurouracil)+ Cisplatin+ Radiotherapy+ Gemcitabin+Carboplatin.	6 9	14 20.9			
	Lymphoma regimen: R-CHOP, ABVD	8	18.6			
	Others: Gemcitabine, BEP					
Stages of Disease	One Two Three Four	29 14 0 0	67.5 32.5 0 0			
Hemoglobin level at the beginning of treatment				12.54	**1.82**	
Hemoglobin level after 4 weeks of treatment				12.23	**1.68**	
BMI at the beginning of treatment	<25 25-29.9 ≥30	15 17 11	34.5 39.1 25.4			
BMI after 4 weeks of treatment	<25 25-29.9 ≥30	16 16 11	37.3 37.3 25.4			

Table 2: Means and Standard Deviations of the Scores on all Subscales of PFS prior to Receiving First Dose of Chemotherapy treatment

Group	Behavioral	Affective	Sensory	Cognitive	Total PFS Scores
All participants					
M	1.27	2.86	3.8	3.9	2.96
SD	1.10	1.57	1.63	1.97	1.45
Highest Score	10	10	10	10	10

(N=43)

Baseline Measurements (pre-treatment)

Piper Fatigue Scale (PFS) Scores

The total PFS scores of participants ranged from 0.75 to 6.2(M=2.96, SD=1.45). Almost all participants scored low on all subscales of PFS prior to receiving first dose of chemotherapy treatment; the behavioral subscale scores ranged from 0.00 to 4.83 (M=1.27, SD= 1.1), affective subscale scores ranged from 1.00 to 6.6 (M=2.86, SD=1.57), sensory subscale scores ranged from 1.00 to 7.8 (M=3.8, SD=1.63), and cognitive subscale scores ranged from 1.00to 8.2 (M= 3.9, SD=1.97), (see Table 2, previous page, for means and standard deviations of the scores on all subscales of PFS prior to receiving first dose of chemotherapy treatment).

Post Treatment Measurements

The total participants' scores on PFS after 4 weeks from receiving first dose of chemotherapy treatment ranged from 1.83-7.08(M=5.26, SD=1.01). Almost all participants scored high on all subscales of the PFS after 4 weeks from receiving first dose of chemotherapy treatment with behavioural subscale that ranged from 0.17 to 6.83 (M=3.51, SD=1.46), affective subscale scores ranged from 2.2 to7.8 (M=5.05, SD=1.27), sensory subscale scores ranged from 2.4 to 8.8 (M=6.19, SD=1.36), and cognitive subscale scores ranged from 1.33to 8.5 (M= 6.31, SD=1.33), (see Table 3, next page, for means and standard deviations of the scores on all subscales of PFS after 4 weeks from receiving first dose of chemotherapy treatment).

Research Question 1 (Fatigue Score).

To answer the first research question "Do patients who receive chemotherapy as a primary treatment for their cancer have statistically higher scores of fatigue as measured by PFSs after 4 weeks from the first dose compared to their scores at the beginning of their treatments? " A paired sample t-test was used for total scores, and each subscale of PFS. Paired sample t-test revealed significant differences between respondents' total mean scores of fatigue pre and post 4 weeks chemotherapy treatment as measured by total PFS questionnaire (t= -2.31, df=42, P<0.05). In addition, significant differences were found between pre and after 4 weeks from receiving the first dose of chemotherapy treatment scores for behavioral, affective, sensory, and cognitive dimensions subscales (t= -2.24, -2.19, -2.4, -2.4, df =42, P<0.05) respectively, (see Table 4 for the results of paired-sample t-test for fatigue scores as measured by PFS).

Research Question 2

"Is there a relationship between fatigue scores (PFS) and selected demographic variables such as age, sex, marital status, Income, level of education, type of cancer, stage of disease, type of chemotherapy, dose of chemotherapy, body mass index, smoking and hemoglobin level among Jordanian patients who receive chemotherapy as a primary treatment for their cancer?". To find the relationship between fatigue score and sociodemographic variables Pearson Product Moment Correlation and Biserial Correlation Coefficient were used.

Pearson Product Moment Correlation Coefficient was used to find the correlation between fatigue scores as measured by PFS and selected sociodemographic variables on a continuous level. Pearson Product Moment Correlation showed a significant negative relationship between fatigue scores as measured by PFS and hemoglobin level (r= -0.04, P<0.01). (See Table 5 for the results of Pearson Product Moment Correlation Coefficient between fatigue Scores as measured by PFS and sociodemographic variables on a continuous level).

Biserial Correlation Coefficient was used to find the correlation between fatigue scores as measured by PFS and selected sociodemographic variables on nominal and dichotomus levels. Biserial Correlation Coefficient showed a significant negative relationship between fatigue scores measured by PFS and sex (r= -0.026, P<0.01). Also, Biserial Correlation Coefficient showed a positive relationship between fatigue scores measured by PFS and type of chemotherapy especially patients treated with Anthracyclin based regimen (r= 0.0398, P<0.05). (See Table 6 for the results of Biserial Correlation Coefficient between fatigue scores as measured by PFS and sociodemographic variables on nominal and dichotomus levels).

Discussion

Regarding question 1

The findings of this study showed that the patients who received chemotherapy as a primary treatment for their cancer have statistically higher scores of fatigue as measured by PFS's after four weeks from the first dose compared to their scores at the beginning of their treatments; and thus demonstrated that fatigue is more related to treatment of cancer than to the cancer and may persist after therapy (12). The reason for increased fatigue scores after 4 weeks from the first dose may be explained based on the fact that the etiology of fatigue in cancer patients is complex, and multidimensional (13). Previous studies (14; 15) found that fatigue precedes, accompanies, and follows most tumours and its treatment. Chemotherapy and radiotherapy cause cellular death (14). As a consequence several chemicals are released into circulation. Such chemicals may increase basal metabolic rate, which may affect energy level (15).

Many cancer patients feel fatigued for several months or even years after their treatment with chemotherapy (16). The previous studies found that fatigue is the most common side effect of cancer treatment including chemotherapy. The mechanism of how chemotherapy causes fatigue is unknown (17) but some studies explained that fatigue related to chemotherapy may be caused by

Table 3: Means and Standard Deviations of the Scores on all Subscales of PFS after 4 weeks from receiving first dose of chemotherapy treatment

Group	Behavioral	Affective	Sensory	Cognitive	Total PFS Scores
All participants					
M	3.51	5.05	6.19	6.31	5.26
SD	1.46	1.27	1.36	1.33	1.01
Highest Score	10	10	10	10	10

(N=43)

Table 4

PFS subscale	Time	N	M	SD	t	df	Sig
Behavioral	Pre-chemotherapy	43	1.27	1.1	-2.24*	42	0.000
	4 weeks after first dose	43	3.51	1.46			
Affective	Pre-chemotherapy	43	2.86	1.57	-2.19*	42	0.000
	4 weeks after first dose	43	5.05	1.27			
Sensory	Pre-chemotherapy	43	3.8	1.63	-2.4*	42	0.000
	4 weeks after first dose	43	6.19	1.36			
Cognitive	Pre-chemotherapy	43	3.9	1.97	-2.4*	42	0.000
	4 weeks after first dose	43	6.31	1.33			
Total PFS	Pre-chemotherapy	43	2.96	1.45	-2.31*	42	0.000
	4 weeks after first dose	43	5.26	1.01			

*P <0.05

Table 5: Results of Pearson Product Correlation Coefficient between Fatigue Scores as measured by PFS and Sociodemographic Variables on a Continuous Level

Sociodemographic Variables	PFS Scores
Hemoglobin level	-0.04**
BMI	0.21

** Correlation is significant at 0.01 level.

the need for extra energy for the process of the healing and repairing body tissues that are damaged by treatment in addition to the building up of toxic substances that are left in the body after using of cancer treatment for killing malignant cells(12).

Research question 2

Of the socio-demographic variables, sex correlates negatively with fatigue. This finding is consistent with many previous studies that showed; women who received chemotherapy reported higher fatigue severity scores than men (18). In this study it could be explained by the differences in the ratio of female participants to male; where most of the study sample are females.

Anemia can occur as a result of the cancer or the cancer treatment (12). Anemia was found to be a common cause of fatigue (12). In this study; the patients with low hemoglobin level perceived a higher level of fatigue than those with high hemoglobin level. This result confirmed the results of previous studies (19). This could be explained by when patients become anemic there is a decrease in the number of circulating red blood cells, the

Sociodemographic Variables	PFS Scores
Age	-0.23
Monthly income	0.063
Sex	-0.026**
Marital status	-0.059
Educational level	-0.042
Job	0.059
Type of cancer	0.74
Smoking	0.34
Type of chemotherapy	0.0398*
Stages of disease	-0.046
Duration time to reach hospital	-0.26
Type of Transportation	-0.272
Dose of Chemotherapy	-0.12

Table 6: Results of Biserial Correlation Coefficient between Fatigue Scores as measured by PFS and Sociodemographic Variables on Nominal and Dichotomus Levels

*Correlation is significant at 0.05 levels.

** Correlation is significant at 0.01 level.

oxygen carrying capacity of the blood is diminished and thus make the patient's heart and lungs work harder and make patients feel tired and weak due to the inadequate supply of oxygen to muscles and other organs (12, 19).

There was a relationship between fatigue and type of chemotherapy (Anthracyclin based regimen). Previous studies demonstrated that fatigue is more related to treatment than to cancer and it may be last after therapy (20). Anthracyclin containing chemotherapy is well known to cause dose dependent progressive cardiac damage, heart failure and cardio toxicities which in turn play an important role in decreased oxygenated blood supply to all body tissues and finalized with fatigue (21). Treatment with the Anthracycline can result in the production of toxic substances as within the cancer cells (20). The more and longer accumulative dose of Anthrocyclin, the more destructive effect on the body (21). There was no available previous studies that assessed fatigue associated with low dose of Anthracyclin.

No relationship was found in this study between BMI and fatigue that could be related to the short duration (four weeks) between pre and post treatment with chemotherapy which is not enough to detect changes in BMI and so changes in perceiving level of fatigue.

Limitations

1. The use of convenience sample and the small sample size were a major limitation since only 43 participants were able to complete this study. So the generalizability of the findings of this study is limited. The inferential statistics performed on these data must, therefore, be interpreted with extreme caution, and no conclusions can be drawn with certainty. Therefore, these limitations were threatening the generalizability of the findings.
2. Validity and reliability of PFS need to be tested in further study.

Conclusions

Despite the limitations of this study, the current and previous research findings, as well as the well-established facts about cancer and chemotherapy, the following conclusions can be drawn:

1. Cancer patients receiving chemotherapy are at risk for considerable treatment related fatigue. Therefore, health care providers should incorporate fatigue in routine assessment of patients who are being treated for cancer or being followed after completing treatment.
2. Fatigue is influenced by hemoglobin level and gender. Therefore, health care providers have an obligation to take these variables into account when caring for cancer patients.

Recommendations

1. Replicating this study with large samples is necessary before making any generalization of the results.
2. Healthcare providers should incorporate fatigue in routine assessments of patients who are being treated for cancer or being followed after completing treatment.
3. Help healthcare providers to consider how people understand, interpret feelings, and sensations associated with fatigue.
4. Teach patients, parents, and health care professionals about the symptoms and impact of

fatigue and the treatable nature of fatigue.

5. Develop new instruments to assess Jordanian cancer patients' fatigue from their cultural perspectives.
6. Assess patient' responses to fatigue taking into consideration verbal and non-verbal responses that vary from one patient to another.
7. Further research is needed to compare levels of fatigue related to chemotherapy and other cancer therapy.

Implications

The following are implications for nursing and medical research, education, practice, and administration based on the results of this study:

1. Health Care Providers should assess fatigue for all cancer patients periodically during their disease and treatment.
2. Course design individualized nursing and medical care plan for their patients taking into consideration fatigue.
3. Health care educators are advised to incorporate fatigue issues in nursing and medical educational programs.
4. Results of this study indicated the need for further studies to explore the effectiveness of nursing and medical strategies used to cope with fatigue among patients in general, and cancer patients in particular.
5. Further studies are needed to assess knowledge, and attitude toward fatigue among nurses and doctors.
6. Hospital administrators must encourage workshops for nurses and other health team members who are responsible for patients' education in strategies used to cope with fatigue.
7. Hospital administrators are encouraged to develop teaching materials like pamphlets, booklets, and brochures about chemotherapy to reduce fatigue in cancer patients and increase their knowledge about it.
8. Establish staff development for nurses in the oncology centers to assist cancer patients to develop fatigue reduction and management programs.
9. Health care administrator should develop an assessment tool to predict patients who are at increased risk for experiencing high fatigue levels during and after cancer treatment.

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