

## The Effectiveness of Nursing Educational Intervention On Improving Fatigue Levels Among Egyptian Patients with Chronic Hepatitis C Virus Undergoing Antiviral Therapy

Sabah Elgendi<sup>1</sup>, Amany Shebl<sup>2</sup>, Wafaa Ismaeil<sup>3</sup>, Mohga Sliem<sup>4</sup>,  
Faye A. Gary<sup>5</sup>

<sup>1</sup>Assistant lecturer of Medical Surgical Nursing Department, Faculty of Nursing, Kafr-ElSheikh University, Egypt

<sup>2</sup>professor of Medical Surgical Nursing Department, Faculty of Nursing, Mansours University, Egypt

<sup>3</sup>professor of Medical Surgical Nursing Department, Faculty of Nursing, Mansours University, Egypt

<sup>4</sup>professor of Medical Surgical Nursing Department, Faculty of Nursing, Kafr-ElSheikh University, Egypt

<sup>5</sup>professor of of Psychiatry and mental health, Frances Payne Bolton School of Nursing, Case Western Reserve University, USA

**Abstract: Background:** Fatigue is a common side effect of antiviral therapy that affects patients' overall wellbeing. **The aim** of this study was to assess the effectiveness of a nursing intervention for reducing fatigue levels among Egyptian patients infected with hepatitis C virus and enrolled in an antiviral therapy program with daily Sofosbuvir (SOF) 400mg and ribavirin (RBV) 1000-1200mg.

**Design:** Quasi-experimental research design was conducted on a convenience sample of 100 patients complaining of fatigue.

**Measurements:** A fatigue severity scale (FSS) measurement was used to assess fatigue levels in pre and post program implementation.

**Results:** Among all subjects (n=100), the results indicated that 62 percent of participants reported having severe base line fatigue scores. The day after the intervention, 49 percent reported severe fatigue levels, 15 and 14 percent reported severe fatigue levels at one and two months after the intervention respectively. Repeated measures (ANOVA) revealed significant correlations between fatigue levels and times of intervention as ( $F=114.437$  &  $p \leq 0.001$ ) with means and standard deviations as ( $M=36.00$  &  $+SD=7.767$ ), ( $M=32.02$  &  $+SD=7.623$ ), ( $M=21.13$  &  $+SD=9.168$ ) & ( $M=15.82$  &  $+SD=10.642$ ) respectively. **Conclusion:** Patients' fatigue levels were high at the baseline. However, the nursing intervention was effective in reducing fatigue levels.

**Keywords:** Antiviral therapy, Egyptian patients, Fatigue levels.

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### I. Introduction

Hepatitis C virus (HCV) remains an important cause of chronic liver disease worldwide. According to the World Health Organization <sup>(1)</sup>, more than 185 million people in the global community have been infected with the HCV. Unfortunately, 350,000 die each year. Importantly, one third of those who become chronically infected are expected to develop liver cirrhosis or hepatocellular carcinoma (CCH) <sup>(2,1,&3)</sup>. The Centers for Disease Control and Prevention (CDC) added that for every 100 persons infected with HCV, approximately 75 to 85 of them will develop chronic hepatitis, and approximately 5 to 20 will have cirrhosis over a period of 20 to 30 years. Of this group, five people will die from liver cancer or cirrhosis <sup>(4)</sup>.

The burden of HCV infection is not limited to the influence of cirrhosis and HCC. Studies have indicated that HCV infection is accompanied with reduced health-related quality of life (HRQOL), even when cirrhosis is absent. In the United States the burden of people infected with HCV has been widely reported <sup>(5,6,7)</sup>. Chronic HCV infection significantly impairs the quality of life, with health-related problems affecting emotional, mental, social, and physical functions <sup>(8&9)</sup>.

Despite the importance of teaching patients and their families, nurses must recognize that patients recently diagnosed with serious chronic conditions may need time to grasp the significance of this severe and life-threatening condition. One of the primary role of nurses is to provide carefully planned and culturally appropriate interventions when providing information to patients and their families <sup>(10)</sup>.

Unfortunately, in 2014 the World Health Organization (WHO) reported that Egypt has the highest prevalence of HCV in the world. In addition, Egyptian patients experience high morbidity and mortality from

chronic liver disease, cirrhosis, and hepatocellular carcinoma. Again in 2014, WHO reported that approximately 20 percent of Egyptian blood donors are anti-HCV positive. Studies pointed out that Egyptians have high prevalence rates of genotype 4 HCV infection, especially in rural areas<sup>(1)</sup>. The use of Sofosbuvir and Ribavirin as a new interferon-free regimen for genotype 4 HCV infection has the potential to significantly impact the incidence, prevalence, and overall burden of HCV<sup>(11)</sup>. This new regimen involving direct-acting antiviral agents (DAAs) has recently been approved for the treatment of geno-type 4 HCV. It is replacing the older regimen of Pegylated-interferon and Ribavirin that was associated with low efficacy and numerous side effects, which led to poor adherence, questionable prognosis, and the deterioration of patients' overall well-being<sup>(12&13)</sup>.

In 2013, the United State Food and Drug Administration approved Sofosbuvir (Sofosbuvir) as a component in a combination antiviral treatment regimen to treat chronic Hepatitis C infection. This regimen has been used to treat genotypes 1, 2, 3, and 4, including patients with hepatocellular carcinoma and those waiting for liver transplants. It is also effective for individuals who are co-infected with Hepatitis C and HIV<sup>(14)</sup>.

These direct-acting treatment medications have produced highly successful rates of a sustained virological response (SVR), which is indicated by negative polymerase chain reaction (PCR) test results among patients with genotype 4 HCV. The Food and Drug Administration<sup>(15)</sup> added that these new treatment modalities have a variety of side effects: decreased appetite, diarrhea, difficulty with moving, fatigue, headache, irritability, lack or loss of strength, muscle aching or cramping, muscle pains or stiffness, nausea, rash or itching skin, and trouble with sleeping. All of these numerous side effects require careful monitoring by nurses and health care professionals<sup>(15)</sup>.

Likewise, recent research reveals that fatigue is the most frequently reported multifactorial symptom<sup>(16,17,18&19)</sup>. Fatigue also has a major effect on the quality of life and daily activities among patients infected with HCV. In clinical studies, fatigue and headache were reported as the most common responses when Sofosbuvir was used in combination with Ribavirin. Moreover, studies have documented that up to 59 percent of people who received Sofosbuvir combined with Ribavirin, and sometimes Peg-Interferon Alfa reported fatigue as a significant side effect<sup>(20)</sup>.

The study of<sup>(16)</sup> have defined fatigue as an overwhelming sense of tiredness, lack of energy and feelings of exhaustion. This aggravating side effect is common in patients with cancer, chronic inflammatory disease, and neurological disease. These patients often rate fatigue as the most difficult problem to manage and as the primary reason for work disability<sup>(16)</sup>. Treatment for fatigue includes non-medical interventions such as rest, relaxation, eating healthy foods and exercising (e.g., walking 30 minutes/day). In addition, the sympathomimetic-like agents and acetylcholine-releasing agents are commonly prescribed as medical treatment for fatigue. These drugs increase attentiveness and decrease restlessness<sup>(21)</sup>.

Nurses are in a key position to carry out health education, because they are the healthcare providers who have continuous contact with patients and their families. Because of their clinical and scientific knowledge, nurses are able to develop disease specific interventions that are both culturally appropriate and cost effective. Nurses have additional opportunities to assess potential problems or side effects of patients' medications and treatments. Nurses education should focus on important dimensions, such as disease prevention and early detection. It should also include information about conserving energy by practicing exercises, following dietary modifications and adhering to a medication schedule while attending to side effects<sup>(22)</sup>. It should also involve discussions about the therapeutic effects of the medication and specific interventions that help alleviate side effects such as walking and dietary changes.

Exercise, with its many forms of physical activity, is one of the most important components of health maintenance. Regular exercise not only maintains a healthy cardiovascular system, but it also enhances liver health. Exercise can lower the risks of numerous types of complications that are associated with HCV infections such as diabetes and depression. It is also important for weight maintenance and loss. Along with a healthy diet, regular exercise is one of the best ways to maintain ideal weight. Conversely, extra weight increases the numbers of fat cells in the liver which can contribute to fatty liver disease and damage. Being overweight is one of the primary causative factors of insulin resistance and type 2 diabetes, which may facilitate the progression of liver disease among patients infected with HCV<sup>(23)</sup>. Fortunately, patients with chronic HCV who are being treated with antiviral therapy have the opportunity to get information about nutrition and diet; it should be emphasized that these two behavioral activities help to improve the overall health status of the patient<sup>(24)</sup>.

In addition, exercising can enhance appetite, relieve side effects of hepatitis C medications, improve the immune system, enhance a sense of well-being, and help the person remain positive and focused on his or her health behaviors. Optimal time for exercise should be between 10 to 30 minutes during the day. Low-impact exercises such as walking or swimming are two of the most effective methods for maintaining health<sup>(25)</sup>. It is recommended that patients should start exercising gradually. For example, it is suggested that they begin with a 10-minute walk, taking rest breaks as needed, and slowly increase activity levels (15 to 30 minutes, 3 to 5 days a week). The United States Department of Veterans Affairs (USDVA)<sup>(26)</sup> stressed that exercise and healthy diet should be considered to maintain health.

Low impact aerobic exercise has apposite effect on reducing chronic fatigue levels even among patients who feel they do not have the energy to go to work or even take a shower. Key benefits also include the improvement of oxygen levels in the blood, and increases in the excretion of endorphins, which make the patient feel more energized. Over time, practicing exercise will make major differences and help patients feel better. This improved health status will reflect on patients' psychological wellbeing, and help them control fatigue symptoms.

The American Association of the Study of Liver Disease<sup>(27)</sup> stresses the importance of well-established therapeutic relationships between patients and providers. These relationships remain crucial for optimal outcomes with new direct-acting antiviral (DAA) therapies and for facilitating access and delivery of medication to patients. While fatigue affects the quality of life (QOL), QOL of those patients can be improved with nursing interventions. These interventions include providing patients with adequate nursing counseling and intensive education. Educational interventions should be applied as a regular portion of the nursing practice, and can be delivered in the form of designed activities, including symptoms management, lifestyle instructions, and behavioral modification<sup>(28)</sup>.

In the current study, a nursing educational program was implemented for a group of male and female patients that experienced fatigue and were under antiviral therapy with Sofosbuvir and Ribavirin. The education program included dietary examples, and it explained the importance of following a healthy diet, including small frequent meals, low salt, low fat, and a high portion of protein daily. A regular schedule for walking and low impact exercise for 30 minutes are also a part of this regimen.

## **II. Methods**

### **Study design, Setting and Subjects**

A Quasi experimental research study was conducted in October 2015 in out-patient clinics at one of the Liver Institutes in Egypt. A convenience sample of 100 adult male and female patients were included in this study according to the following criteria: 1) Adult conscious male and female patients, age ranged between 20 to 60 years, diagnosed with HCV and are receiving Sofosbuvir therapy 400mg once/day; 2) self-reported mild to moderate or severe fatigue levels; and 3) were not using any measures for managing fatigue. The sample size was calculated with G power<sup>(29)</sup> and calculated to be 100 patients but 95 patients completed the study.

#### **Measures**

To collect data, two measures were utilized. The first one consisted of two parts; part one included participants' socio-demographic characteristics, while the second part was related to participants' clinical data and items about self-reported diet and exercise behaviors. The second measure was Fatigue Severity Scale (FSS), which was used to assess fatigue levels for Egyptian patients. This tool was adapted from<sup>(30)</sup> and translated into an Arabic version. It consisted of nine statements in a Likert Scale format. The Likert scale system has been modified by the researcher from a 1-7 item scale to a 1-5 item Likert scale to avoid subjects' confusion and enable them to choose the suitable answer for their condition. Thus, the Likert Scale became 1= strongly disagree (low fatigue level), 2= disagree, 3= undecided, 4= agree while 5= strongly agree (high fatigue level). The researcher read each statement carefully and circled a number from one through five that best described the participants' degree of agreement with each statement. The total score ranges were from 9-45. Scores between 13.5 and 22.5 indicated mild fatigue, while scores between 23 and 31.5 indicated moderated fatigue. Scores greater than 31.5 reflected severe fatigue.

#### **Procedure**

A structured face-to-face interview was implemented four times during the collection of the data. Data was collected at the baseline, immediately after the nursing intervention, and again one month after the nursing intervention and two months after the nursing intervention.

#### **Statistical analysis**

Data was collected, coded, revised, cleaned and entered to statistical software Statistical Package for the Social Sciences (SPSS) version 23<sup>(31)</sup>. The statistical analysis using frequency distribution was used to determine subjects' characteristics and frequency of fatigue levels among the subjects. The 9-item responses in the FSS were combined into one total score per time / point by calculating the mean of all items. Analysis of variance (ANOVA) was used to determine the relationship between total fatigue mean scores, in relation to four time points in order to evaluate the effectiveness of the nursing intervention.

#### **Ethical considerations**

The research protocol and measures were submitted to the Ethical Committee of the Faculty of Nursing, Mansoura University, Egypt. Approval and official permission to conduct the study was received from the university and hospital administrators (2015). The purpose of the study and specific information about the

research were shared with all patients using the same guide. The researcher emphasized that participation in the study was entirely voluntary. Anonymity and confidentiality were assured by removing any identifying information from the collected data through using a coding system that helps assure that the names of the participants will not be known to anyone, including the researcher. Oral consent from patients to participate in the study was one of the accepted methods of approval for individuals who wished to become engaged in a research program. At the time of data collection, oral consent was the accepted standard for patients' participation and research (2015).

### III. Results

#### Subjects characteristics

The study subjects consisted of 100 male and female adult participants, 95 of them completed the educational program. Table 1 shows that: Their ages ranged from 20-60 years. Most of the population was between 31 and 40 years of age, (38 %) and 13 % was between the ages of 5 and 60 years of age. The majority (53 %) of participants were male and (77 %) were married. More than half of the subjects resided in rural areas (54 %) and (46%) lived in urban settings. Participants' educational levels indicated that most of the individuals were able to read and write at (72 %), while (28 %) could not read or write. On the other hand, more than one third of participants' (39 %) worked in non-governmental agencies, while (30%) were housewives, and only (12%) worked in governmental agencies. Finally, (19 %) were unemployed. In addition, (42 %) of subjects self-reported that they were smokers.

**Table 1: Frequency distribution and percentages of socio-demographic characteristics (N=100)**

Variables	Frequency	Percent
Age / Yrs.		
20-30	21	21%
31-40	38	38%
41-50	28	28%
51-60	13	13%
Gender		
Male	53	53%
Female	47	47%
Residence		
Rural	54	54%
Urban	46	46%
Marital status		
Married	77	77%
Not married	23	23%
Educational level		
Read and write	72	72%
Not read or write	28	28%
Employment		
Governmental	12	12%
Nongovernmental	39	39%
Not employed	19	19%
House wife	30	30%
Smoking		
Smokers	42	42%
Non smokers	58	58%

#### Fatigue levels among the subjects

At the time of base line data collection, participants' fatigue levels were recorded. The results indicated that the majority of the subjects (66%) reported severe fatigue levels; almost one third (32%) reported moderate fatigue; while a small group (2%) reported mild fatigue. When the fatigue level was assessed immediately after the nursing educational program implementation, results indicated that almost half of the sample (49%) reported that they were suffering from severe fatigue while (8%) reported mild fatigue. One month after the nursing intervention program 15 and 41 percent of the participants reported severe and mild fatigue levels respectively. At two months after the educational program, 14 percent reported severe fatigue levels and 5 percent reported mild fatigue levels. In addition, at two months 62 percent of participants reported less than mild fatigue.

**Table 2: Fatigue levels at four data collection time points**

	Fatigue level Baseline*	Fatigue level post1**	Fatigue level post2***	Fatigue level post3****
	N(%)	N(%)	N(%)	N(%)
Mild fatigue level	2	8	41	5
Moderate fatigue	32	43	20	14

level				
Severe fatigue level	66	49	15	14
No fatigue (less than mild score)	Zero	Zero	19	62
Missing data	Zero	Zero	5	5

- \*base line — before nursing educational program implementation
- \*\*Post 1—immediately after nursing educational program implementation
- \*\*\*Post 2— one month after nursing educational program implementation
- \*\*\*\*Post 3— two months after nursing educational program implementation

Differences between total fatigue mean scores in relation to four data collection time points  
 As reported in Table 3, there was a statistically significant difference between the total fatigue mean scores in relation to the four data collection time points as ( $F_{114.437}$ ;  $p < 0.001$ ).

**Table 3: Total fatigue mean scores in relation to four data collection time points**

Time	Total Fatigue Scores				F	p
	Baseline (pre)	Post (1)	Post (2)	Post (3)		
	M±SD	M±SD	M±SD	M±SD		
	36.00 ±7.767	32.02 ±7.623	21.13±9.168	15.82 ±10.642	114.437	<.001

#### IV. Discussion

Worldwide, fatigue has been documented as one of the most common complaints among patients with chronic HCV. It can produce intolerable side effects among individuals who are receiving antiviral therapy treatment<sup>(32&33)</sup>. Age, gender, marital status and residence suggested that more than half of the subjects were males, aged 30 to 60 years, married, and living in rural areas. This study is supported by similar results obtained by<sup>(34)</sup>, who reported that more than 75% of the individuals diagnosed with HCV infections in the Egyptian population were male, uneducated, 30 years old and above and resided in rural areas.

Regarding fatigue levels, the current study demonstrated that more than 50% of the subjects reported severe fatigue levels at the baseline, at Post-program implementation, slightly less than half of the participants reported decreased levels of fatigue (see Table 2). The differences in fatigue levels mean scores in participants undergoing antiviral therapy compared with each other in relation to four time points of data collection were statistically significant (see Table 3). Importantly, it is evident that the severity of fatigue levels has decreased among the participants. These results may also reflect the effectiveness of the diet and exercise education which were major components of the nursing educational intervention program.

Eating regularly balanced meals means eating at least 3 meals a day. It helps keep patients' energy levels up when they eat small meals or snacks at least every 3 to 4 hours. When patients are receiving hepatitis C treatment, eating often also can help prevent nausea which is sometimes an annoying side effect of the medicine. Balanced meals include a variety of foods from all four food groups that supply the body with important nutrients such as: whole-grain breads, cereals, vegetables and fruits, dairy products, meats, fish, dried beans, soy, nuts, and eggs<sup>(35)</sup>. Importantly, walking is an exercise that can be easily implemented among those groups of patients. This type of exercise is appropriate, available and all people can participate on a daily basis. Walking is a common activity in Egypt, for people typically walk from one destination to another.

#### V. Conclusion

The study concluded that the severity of fatigue levels as a side-effect of HCV treatment therapy can be alleviated by a nursing educational program. Severe fatigue levels significantly improved among those participants as a result of the nursing educational program implemented in this study. The major components of the program were: walking 30 minutes a day, as well as following a healthy diet. It is important to increase patients' awareness and knowledge of their disease by providing nursing educational intervention programs. In essence, these will help patients overcome their fatigue levels and improve their overall quality of life.

#### VI. Implications For Nursing Practice

Diet is one of the most important interventions that should be emphasized by the nurse in order to decrease fatigue and maintain health. These findings are in agreement with<sup>(36)</sup>, who emphasized that patients should be educated about the significance of diet and following healthy lifestyles. In addition, the current study findings also indicated that practicing exercise on a regular basis, such as walking at least 30 minutes per day on most days, had a positive impact on decreasing the fatigue levels of patients with chronic hepatitis C that were also undergoing antiviral therapy<sup>(37)</sup>.

## VII. Limitations Of The Study

Although there were significant differences between fatigue levels in relation to four timepoints, the researcher did not assess the Survival Virologic Response (SVR) to antiviral therapy (tested by PCR) during the time at which the study was conducted. SVR could be an extraneous factor in patients' assessment of their own fatigue levels. For instance, when patients achieve a sustained SVR during the treatment period, it improves their psychological state, which may play a role in relieving or decreasing fatigue.

## Conflict Of Interest

The authors declare no conflicts of interest.

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