Fatigue Levels among Patients with Chronic Hepatitis C Undergoing Antiviral Therapy

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Abstract: The objectives of this study are: to assess fatigue levels among patients infected with the hepatitis C virus (HCV) and undergoing 24 weeks of daily antiviral therapy with Sofosbuvir (SOF) and ribavirin (RBV). Design and sample: A descriptive study was conducted on a convenience sample of 100 patients with chronic Hepatitis C undergoing antiviral therapy in outpatient clinics in Egypt. Fatigue was assessed using the Fatigue Severity Scale (FSS). Results: Among all participants (n=100), 66 percent reported having severe fatigue levels while 32 percent reported having moderate fatigue levels. Conclusion: our study confirms that fatigue was the most common side-effect among patients with chronic HCV and undergoing antiviral therapy. Nurses can use these findings to develop programs to decrease fatigue levels among patients infected with HCV patients.
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1. Introduction

Hepatitis C virus (HCV) is a universal communal health challenge which is preventable. It remains an important cause of chronic liver disease worldwide, and currently it is the most frequent cause of liver related morbidity and mortality (WHO,2016; Abd-Elwahab, 2016; Wang, et al,2014; Guerra, et al, 2012; Chemaitelly, Abu-Raddad & Miller, 2013; Garenne, Mohamed, Fontanet,2012). More than 185 million people over the world have been infected with the HCV, of whom 350,000 die each year (WHO, 2014; Averhoff, Glass, & Holtzman, 2012). Nurses have an important role in assessing fatigue and quality of life levels during antiviral therapy. When nurses work together with patients and other health care professional, they can proactively develop effective comprehensive educational programs and plans of care to increase optimal outcomes and enable patients to overcome these challenges(Roles et al., 2017).

After 20 years of infection, the risk for developing cirrhosis among patients with chronic HCV is estimated at around five to fifteen percent, this estimate varies among studies across countries (Lam, Henry & Younossi, 2014). Once the progression to cirrhosis has occurred, the annual risk of hepatocellular carcinoma (HCC) increases from one to seven percent, decompensate liver disease increases to five percent, and liver-related death rise approximately to two percent. End-stage liver disease and HCC that is related to HCV have become the primary cause for liver transplantation worldwide (Lam, Henry & Younossi, 2014).

Unfortunately, Egypt has the highest prevalence of chronic HCV in the world. In this nation more than 90 percent of the patients are infected with the hepatitis C virus which is known as genotype four (Doss et al., 2015). This high rate has created many challenges for all segments of healthcare system in caring and treating people with HCV in Egypt. Demographics represent a historically high number of cases of HCV infection. This fact distinguishes Egypt from other global communities (Mohamoud, et al, 2013; Gomaa & Crossey, 2017)

The use of older pharmachological agent such as pegylated-interferon (Peg IFNa) and Ribavirin (RBV) are known to have low success rates with numerous side effects which might lead to poor adherence and impairment of the patients' well-being. Furthermore, the research findings indicate that the prognosis of patients undergoing therapy for chronic hepatitis C and, for those who have progressed to the point of decompensate liver cirrhosis is poor (WHO, 2016; Lam, Henry, & Younossi, 2014). New regimens involving Direct-Acting Antiviral Agents (DAAs) have been accepted for the treatment of genotype four HCV. These new regimens appear to offer higher success rates of sustained virologic response (SVR) in initial treatment as well as previously treated patients with genotype four HCV. However, few patients have benefited from these regimens and data concerning

their efficacy and safety are inadequate and questionable (Muir, 2014; Lam, Henry & Younossi, 2014).

Interestingly, the development of an interferon-free regimen for treating genotype four HCV infections has the possibility to reduce the incidence, prevalence, and overall burden of HCV in Egypt and other global communities. Researches have suggested that this approach may decrease the required frequency of monitoring patient's drug safety, and could facilitate the use of these agents in treatment of chronic hepatitis C in rural areas in Egypt. Recall that the higher incidence and prevalence of genotype four HCV is in exist in rural areas, but it exists in urban communities as well (Guerra, et al, 2012; Abdel-Ghaffar, Sira, & El Naghi, 2015; Hathorn, & Elsharkawy,2016; Ruane, et al, 2015).

The American Association for the Study of Liver Diseases (AASLD), The European Association for the Study of the Liver (EASL), and World Health Organization (WHO) updated the guidelines for the treatment of genotype four HCV. These new guidelines contain Sofosbuvir administration in combination with PegIFNa and RBV for twelve weeks or an interferon-free regimen of Sofosbuvir in combination with RBV for 24 weeks (Ruane et al., 2015, AASLD,2014, EALS,2014, & WHO,2014).

Recently, AASLD and Infectious Disease of Society of America (IDSA) updated guidelines for individuals beginning treatment for HCV genotype 4 infection who have no cirrhosis and others who have compensated cirrhosis. These recent treatment regimens are daily fixed-doses for 12 weeks and are determined by virus class and level of evidence as follows: combination of Paritaprevir (150 mg)/Ritonavir (100 mg)/ Ombitasvir (25mg) and weight-based Ribavirin for Class I, Level A. Or Sofosbuvir (400 mg)/Velpatasvir (100 mg) for Class I, Level A. Or Elbasvir (50 mg)/Grazoprevir (100 mg) for Class II a, Level B. For patients who are Class II a, Level B Ledipasvir (90 mg)/Sofosbuvir 400 mg were recommended(Guidance, 2016).

Sofosbuvir is a prescribed oral medication taken once per day. It is a nucleotide analog polymerase inhibitor to be used in combination with Peginterferonalfa and Ribavirin or Ribavirin. The active ingredient in this 400 mg tablet is Sofosbuvir (Food and Drug Administration (FAD),2014). Fatigue is the most frequently reported multifactorial symptom and one of the known treatment side-effects of liver disease which may have a major effect on quality of life and daily activity among HCV chronically infected patients. In clinical studies, fatigue and headache were reported as the most common responses when Sofosbuvir was used in combination with Ribavirin (Doss et al., 2015). While the most common outcome when Sofosbuvir was used in combination with Peginterferonalfa and Ribavirin were fatigue, headache, nausea, insomnia and anemia. (FDA, 2014; Robinson, 2016).

In this study, we assessed fatigue levels among Egyptian patients undergoing treatment with free interferon (INF) therapy (Sofosbuvirplus ribavirin).

The study results should expand the signs of effective implications on research, practice, education, nursing care and approaches to patients' education. Importantly, nurses and other health care professionals may be able to develop new approaches that provide support for individuals complaining of HCV with reported fatigue. Findings of this study might also improve patients' quality of life, enhance their capacity to function and address their activities of daily living.

2. Methods

Study design, sample and setting

A descriptive correlational study was conducted at outpatient clinics in Kafr El Shikh, Egypt. A convenience sample of 100 adult male and female patients were included in this study. All patients met the following criteria: adult male and female patients diagnosed with genotype 4 HCV, aged between 20 - 60 years, diagnosed with HCV and receiving Sofosbuvir therapy 400mg once per day, had mild, moderate, or severe fatigue severity scores; and did not use self-management intervention in treating fatigue. Exclusion criteria included: pregnant women, patients with severe renal impairment, and individuals who could not participate in verbal interaction with the researcher.

Data collection measures

Three research measures were used for this study. Asocio-demographic data sheet was developed to collect specific characteristics about the sample. The Arabic version of fatigue severity scale (FSS) was administered to the subjects to measure their fatigue scores (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989). FSS consisted of nine statements in a Likert Scale format. The researchers carefully read each statement to the patients and circled the answers that they selected from the scale that best described the agreement with each statement. The researcher decided to read all items of the FSS, this decision was made for several reasons, including the fact that some of the patients may have had difficulty in comprehending the items on the measures that were presented in the Likert scale format. The researcher was familiar with the Likert scale and frequency of its use. However, individuals of other cultures and countries might not be conversant with scale (Ezisay,2017). In fact, it is reported that individuals who are not familiar with the scale might not report

the appropriate responses, but instead could select the least problematic response (Ezisay,2017). The total possible scores ranged from 9-45; however, scores between 13.5 to 22.5 indicated mild fatigue, while scores between 23 to 31.5indicated moderate fatigue; and scores greater than 31.5 suggested severe fatigue. FSS has been used for patients with sclerosis and systemic Lupus erythematosus. 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 responses that most closely reflects their condition. The scale used was as follows: 1= strongly disagree, 2= disagree, 3= undecided, 4= agree while 5= strongly agree.

Procedure

The researcher determined that face- to- face interviews with the patients would be the best approach for collecting accurate and complete data. patients were interviewed and asked about their sociodemographic characteristics. Fatigue levels were assessed using the adapted (FSS) questionnaires. Using Arabic FSS, patients were asked to select a score between one (completely disagree) and five (completely agree) to each of the nine FSS items. The scale was designed to rate the extent of fatigue symptoms and their impact on patient functioning including for example: 1-My motivation is lower than when I am fatigued, 2-Exercise bring on my fatigue, 3-I am easily fatigued, 4- Fatigue interfere with physical fatigue, 5- Fatigue causes frequent problem for me, 6-My fatigue prevents sustained physical functioning, 7-Fatigue interfere with carrying out certain duties and responsibilities, 8- Fatigue is among my three disabling problems and 9- Fatigue interfere with my work, family or social life. A higher score indicated a greater degree of fatigue.

Statistical analysis

Data were collected, revised, coded, and entered into the Statistical Package for the Social Sciences (SPSS), version 23(Files et al., 2016). Statistical analysis was done using frequency distribution for all variables. The nine-item responses in the FSS were combined into total score by calculating the total mean of all items.

Ethical considerations

The study was approved by the Ethics Committee of Faculty of Nursing, Mansoura University, Egypt. Oral consent from the subjects was approved by the university at the time data were collected. The informed consent form was carefully discussed with each of the subjects, and they were given the opportunity to ask questions before the interview process begin. after the subjects stated that they understood the purpose of the study and that they willing to participate, the interview began. All data were coded to help ensure anonymity, privacy and confidentiality of the information.

3. Results

Participant Demographics

The study participants consisted of 100 adult patients and their ages aged between 20-60 years. Table 1 summarizes their characteristics as the following: Regarding age, more than one third (38 percent) were between 31-40 years, while (13 percent) ages ranged from 51-60 years. Regarding gender, the majority of the sample (53 percent) were female, while (47 percent) were males. The majority of the subjects were married (77 percent), while (23 percent) were not married. In relation to residence, more than half of the subjects (54 percent) lived in rural communities while (46 percent) lived in urban communities. Regarding educational level, (72 percent) were able to read and write in Arabic, while (28 percent) were not able to read and write in Arabic. Employment suggested that more than one third of the sample (39 percent) were non-governmental workers, (30 percent) were housewives, and (12 percent) worked for the Egyptian government. Finally, (19 percent) were unemployed. More than half (58 percent) were non cigarette smokers, while more than one third of the subjects (42 percent) were cigarette smokers.

Table 1: Frequency distribution and percentage of socio-demographic characteristics among the studied subjects (N=100)

Variables	N (N = 100)	Percent
Age / Yrs.		
20-	21	21
31-	38	38
41-	28	28
51-60	13	13
Gender		
Male	53	53
Female	47	47
Residence		
Rural	54	54

Variables	N (N = 100)	Percent
Urban	46	46
Marital status		
Married	77	77
Single	23	23
Job		
Governmental job	12	12
Nongovernmental job	39	39
No work	19	19
House wife	30	30
Smoking		
Yes	42	42
No	58	58
Educational level		
Read and write	72	72
Can't read and write	28	28

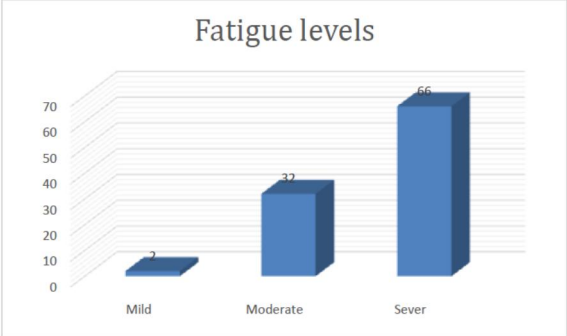

Figure 1; Frequency Distribution of Fatigue Level Among Studied Subject (N = 100)

Two thirds (66 percent) of the subjects reported severe fatigue levels. while 32 percent reported mild levels. See Figure 1.

4. Discussion

Fatigue is perhaps the most common symptom among patients with chronic hepatitis C virus and it is a troublesome side-effect associated with the prescribed therapies (Sarkar, et al, 2013). In addition, the treatment of this chronic condition may temporarily worsen HRQOL because of the common adverse effects such as fatigue (Abd El-Wahab, 2016). Patients who enrolled in this study self-reported having some degree of fatigue; one third reported moderate fatigue and more than half of the them rated their fatigue as severe.

These study results are similar to the findings of other research. Specifically, researchers studied the Efficacy of Sofosbuvir Plus Ribavirin in Veterans in United States with Hepatitis C Virus Genotype 2 Infection, Compensated Cirrhosis, and multiple comorbidities. Their results indicated that the most common adverse events were fatigue, anemia, nausea, and headache (Monto et al., 2016). As expected, fatigue became more troublesome during the antiviral therapy, and worsened during the first few weeks of the therapeutic regimen (Sarkar, et al, 2012).

Limitations of the study:

Several limitations are associated with this study. First, because participants from rural and urban communities and depending on public transportation. They reported concern about transportation and time. second, the other limitation is that the patients` education level delayed the capacity for them to read, comprehend and understand the questions. Third, it was observed that some men had a sense of embarrassment that was associated with the limited capacity to read and understand the questions.

Recommendations for further study:

Further study should be done with a larger group of patients who are receiving different prescribed therapeutic regimens. Comparison among different groups that consider age, gender, socioeconomic status and other demographic variables needed to be conducted. Studies about more effective therapies should be done for genotype four. Finally, as HCV is one of the most common conditions in Egypt, and its high levels of patients` dissatisfaction along with the exaggerated cost of treatment, researches needed to improve the quality of life and decrease mortality and morbidity rates.

Conclusions

This study concluded that that fatigue was not only the most common symptom of chronic HCV in northern region in Egypt, but also the most common side-effect for patients with HCV. They are more likely to have high fatigue scores. These findings can help nurses and other health care providers to better plan treatment programs for patients with HCV as well as to improve HRQOL.

Conflicts of interest.

The authors declare no conflicts of interest.

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