Effect of Educational Nursing Interventions Program on the Severity of Extrahepatic Manifestations among Patients with Chronic Hepatitis C Virus

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Abstract

Background: Many studies recommend that nursing interventions such as maintaining adequate hydration and light to moderate exercise, as well as rest keep HCV patients who suffer from extrahepatic manifestations tend to feel better. The nurses have a major role in the developing and implementing an effective nursing educational interventions for such sufferers. **Aim of the study:** This study aimed at identifying the effect of an educational nursing interventions program on the severity of extrahepatic manifestations among patients with chronic hepatitis C virus. **Design:** A quasi-experimental research design**. Sample:** Forty adult patients with HCV infection were assigned randomly. **Setting:** The present study was conducted at the Outpatient clinics of Shark El Madinah hospital, Alexandria, Egypt. **Tools:** Three tools were used for data collection. **Results:** this study illustrated that all of the knowledge scores of the studied patients with hepatitis C virus were highly statistically significant improved post implementation of the educational program. There were no significant differences between score of nursing interventions with scores of severities of extrahepatic manifestations pre and 4 weeks post implementation of the program. While there were significant differences between them 8 weeks post implementation of educational nursing program. **Conclusion:** this study exemplified that all of the knowledge scores of the studied patients related to chronic HCV infection, its extrahepatic manifestations and nursing interventions to deal with these manifestations were highly statistically significant improved post implementation of the educational program. However, there is no significant difference between the scores of severity of extrahepatic manifestations among the studied patients pre and post implementation of educational program. **Recommendations:** it is recommended that educational nursing intervention program should be applied to all patients with chronic hepatitis C virus in suitable environment for teaching and supported with more audiovisual materials.

Keywords: Nursing Interventions, Extrahepatic Manifestations, Chronic Hepatitis C Virus

Introduction

Chronic hepatitis C virus (HCV) infection is a major global health problem affecting 1% of the world population **Waked, et al, (2020).** Egypt has a unique HCV prevalence pattern that is not comparable with those of its eastern Mediterranean neighbors **Gomaa, et al, (2017).** HCV prevalence rates in Egypt reach 13% of the population equating to an estimated 12 million Egyptians. Around 8 million of them are living with chronic hepatitis C without or with cirrhosis or liver cancer. In Egypt, HCV is not only a complicated disease process but a serious public health, economic, and social problem that exceeds the margins of biomedicine **Kamal, & Abdelhakam (2018).**

Beyond hepatic complications associated with HCV infection there are non-hepatic complications which affect many other organs **Sherman & Sherman (2015).** HCV infection causes a variety of systemic disorders (extrahepatic manifestations); some of which bear more severe morbidity than the liver disease itself. Extrahepatic manifestations (EHMs) represent a wide spectrum of disorders,

ranging from the presence of insignificant autoantibodies to diseases affecting a variety of vital organ systems **Jukić, & Kralj, (2017).** Seventy percent of chronic HCV patients suffer from **EHMs Kalantari, et al, (2018).** Furthermore, EHMs increase the mortality rate among patients with chronic HCV than those without HCV infection **Cacoub (2016).**

EHMs can be classified according to affected organs into cardiac, thyroid, endocrine, renal, ophthalmic, musculoskeletal and cerebral manifestations. Cardiac manifestations include coronary artery sclerosis and other coronary diseases while the thyroid manifestations are thyroiditis, Graves ' disease and thyroid cancer. In addition, renal disorders are glomerulosclerosis and renal insufficiency but on the ophthalmic are Mooren's ulcers, and sicca syndrome. Furthermore; HCV may affect endocrine system and cause diabetes and insulin resistance. On muscles and joint; it produces myalgia and arthralgia. HCV affection can extend to brain tissue causing fatigue and depression which is mostly affect quality of life of HCV infected patients **Cacoub, (2016).**

Arthralgia and myalgia are one of the most common EHMs of HCV infection **Tengan, et al, (2017).** Although symptoms can be disabling, the prognosis typically is pleasant. Patients who have chronic inflammatory arthritis with an unknown cause should be evaluated for HCV infection. The exact mechanism by which HCV infection triggers arthritis has not been determined, but it may be result from a local inflammatory response to synovial tissue by viral invasion or by deposition of cryoglobulin-induced immune complexes in synovial fluid **Tung, et al, (2018).**

Neuropsychiatric manifestations are one of EHMs that have direct and important effect on quality of life of patients with chronic HCV infection. These manifestations include but not limited to chronic fatigue, depression, and cognitive impairment. Up to 50 % of patients with HCV infection can develop a variable combination of clinical or subclinical neuropsychiatric manifestations and neuropsychological/psychiatric manifestations **Kuna, et al, (2019).** Moreover, **Dirks, et al. (2017)** considered chronic fatigue is one of the most disabling symptoms of HCV infection

The intracerebral neurobiological changes associated with HCV may potentially explain such symptoms as depression and fatigue. These changes may arise from infiltration of the brain by peripherally induced cytokines, as well as direct neuropathic effects of HCV particles that penetrating the blood-brain barrier. HCV-associated intracerebral changes include upregulated inflammatory responses, altered neurotransmitter levels, hormonal dysregulation, and release of neurotoxic substances. These may subsequently lead to abnormal neuronal conduction and function in areas of the brain governing affective responses, emotional processing, motivation, attention and concentration **Yeoh, et al, (2018).**

Although the current antiviral agents may result in complete clearance of HCV which decrease the risk of these manifestations, it was found during course of therapy that these manifestations may be increased **Kuna, et al (2019).** Moreover, although direct-acting antiviral medications lead to high rates of HCV clearance, some neurocognitive deficits may persist **Yeoh, et al (2018).** This situation set health care providers in dilemma.

Many nursing interventions are of help for some EHMs without any side effects. Many patients respond positively to rest, relaxation techniques, warm bath and walking **Kuna, et al (2019).** In addition, **Sung et al (2011)** mentioned that certain interventions such as maintaining adequate hydration and light to moderate exercise keep HCV patients tend to feel better. Hence the nurses have a major role in developing effective nursing interventions program for patients with HCV who suffer from EHMs to manage these disabled symptoms and assist patients in performing effective care.

Aim of the study:

The present study aims to evaluate the effect of educational nursing intervention program on the severity of extra hepatic manifestations among patients with chronic hepatitis c virus Infection

Hypothesis of the study:

Patients who receive educational nursing intervention program will exhibit decreased severity of extra hepatic manifestations than those who would not receive it

Methodology

Materials

Research Design:

Quasi experimental research design was utilized.

Setting:

The present study was conducted at the Outpatient Clinics **of Shark El Madinah** hospital, Alexandria, Egypt.

Subjects:

Forty adult patients with HCV infection were assigned randomly. The program of **Epi Info 7** was used to estimate the sample size using a population size of 2400 in 2021, prevalence rate of 10 %, confidence 95% and acceptable error of 10 %. The minimum sample size required is 34 patients.

- **The study group** was subjected to a designed nursing intervention program in addition to the routine hospital care.
- **Inclusion criteria:** The subjects were selected according to the following criteria:
  - Adult patients 21-60 years.
  - Free from any other associated disease as uncontrolled diabetes, hypertension.
  - Able to communicate verbally, and able to follow instructions.
  - Willing to participate in the study.

Tools of the study:

Three tools were used for data collection based on a thorough review of relevant literature

Tool One: Hepatitis C Virus patient's knowledge structured interview schedule:

This tool was developed in Arabic language by the researchers after the review of relevant recent literature to assess patients' knowledge related to HCV, EHMs, as well as nursing interventions of these manifestations. It was divided into two parts:

Part I: Sociodemographic characteristics of patients.

Part II: patients' knowledge related to HCV disease, EHMs, and their nursing interventions.

Scoring system: Patients' knowledge answers were scored on 3 points Likert scale (1= no, 2= not sure, and 3= yes). After that all scores were summed up together for each patient. Total score was classified as the following:

- More than 70% of the total patients' knowledge scores were considered as **good**.
- Less than 70% up to 50% of the total patients' knowledge scores were considered as **fair**.
- Less than 50% of the total patients' knowledge scores were considered as **poor.**

Tool Two: Extrahepatic manifestations, severity, and nursing interventions of them structured interview schedule: This tool was developed in Arabic language by the researchers after the review of relevant recent literature to assess current EHMs, their severity and care performed by the patients for these manifestations, and its effectiveness. It was consisted of three parts as the following:

Part I: Extrahepatic manifestations. This part aims to collect data about EHMs experienced by those patients

Part II: The severity of EHMs. This part was used to determine the severity of each symptom on a 5-point Likert scale, with responses 1(not at all), 2 (A little), 3 (moderately severe), 4 (quite a bit) to 5 (extremely severe).

Part III: Nursing interventions for experienced manifestations

This part was concerned with describing nursing interventions to deal with each symptom and the effectiveness of each according to the following (0 = not used, 1

used but not relief, 2=used, partially relieved, 3=used, completely relieved).

Scoring system: All scores were added for each patient. Total score was classified as the following:

- **From zero to less than 30%** of the total patients' extrahepatic manifestations severity scores was considered as **mild.**
- **From 30% to less than 70%** of the total patients' extrahepatic manifestations severity scores was considered as **moderate**.
- **From 70% up to 100%** of the total patients' extrahepatic manifestations severity scores were considered as **severe.**

Tool Three: Fatigue Severity Scale:

It was developed by **Krupp et al** (1989) and was translated into Arabic by the researcher, to measure fatigue severity. It consisted of nine statements concerning with response to fatigue that includes decreased motivation associated with fatigue, how fatigue affects exercise, physical functioning, easily fatigability, frequent problems associated with fatigue, carrying out duties, interfering with work, family, or social life with score ranged from 1-7, where 1 indicates strongly disagree (low fatigue level) and 7 indicates strongly agree (high fatigue level).

Scoring system: The total score was ranged from 9 - 45. From 13.5 - 22.5 is categorized as mild fatigue level, and from 23-31.5 is categorized as moderate, while more than 31.5 – 45 is categorized as severe fatigue level. The original likert scale ranges from 1-7 for each item. The scoring system was readjusted to likert scale 5 ranging from 1-5 here 1 indicates strongly disagree (low fatigue level) and 5 indicates strongly agree (high fatigue level) using the following formula: **Adjusted score = Patient Score** × 45 / 63.

Method

1.Before conduction of the study an official letter from the faculty of nursing was submitted to the general director and head of the hepatic outpatient clinics of Shark El Madinah Hospital to take approval for data collection. Permission to carry out the study was obtained from the director of the chosen setting after explanation of the purpose of the study.

2.The study tools were developed by the researchers

3.The study tools and the program were tested for content validity by a jury of nine experts in medical surgical nursing specialty and the necessary modifications were carried out accordingly.

4.Reliability of tools were done using Cronbach Alpha Test. Reliability coefficient for tool I was 0.784, for part I of tool II was 0.7 while part II and III of it was 0. 78 and for tool III was 0.87.

5.A pilot study was conducted on 4 patients for testing clarity; feasibility and applicability of the developed tools and modifications were done accordingly.

6.Sample size: Based on **Epi Info 7** program, a sample of 40 adult patients with HCV infection is assigned randomly.

- **The study patients were** subjected to the designed nursing interventions program in addition to the routine hospital care (not include any educational nursing interventions).

7.Data collection:

After securing the administrative approval, the data collection was started, and continued for a period of 8 months from January to August 2021.

The study was carried out in four phases:

I. Assessment phase:

- **Initial assessment** was carried out using the three tools to collect baseline data and to identify patients' needs for educational nursing interventions program.
- **Subsequent assessment** was done 4 weeks, and then 8 weeks post implementation

of the program in order to evaluate patient's progress.

II. Planning Phase:

▪ An educational nursing interventions program was designed by the researchers based on assessment phase and recent literature review related to HCV, EHMs, and their management.

▪ The designed program included goals, contents, priorities and expected outcomes that were tailored to patients' individual needs and problems.

▪ Illustrative booklet containing the designed nursing interventions program was distributed to each patient as a reference at the first session of the implementation phase.

III. Implementation phase:

▪ The developed educational program was implemented and applied individually in the outpatient clinics using verbal instructions and was supported by written booklet as an illustrative guide for more clarification. Patients were asked to bring one of the family members to attend the education sessions for reinforcement of the prescribed instructions.

▪ Educational nursing interventions program was consisted of three consecutive sessions; each session was conducted in around 45 minutes; nursing interventions sessions begin just patient's admission to outpatients' clinics as the following:

◆ **first session** included the following:

▪ **HCV infection**

- Definition of HCV infection
- Risk factors
- Signs and symptoms
- Mode of transmission
- Diagnosis
- Complications.

▪ **Extrahepatic manifestations of HCV**

- Cardiovascular manifestations
- Musculoskeletal manifestations
- Endocrine manifestations
- Renal manifestations
- Immune manifestations
- Neuropsychiatric manifestations

❖ **Second session** included the following content:

Nursing interventions to relive EHMs of HCV. Patients were asked to repeat learned nursing interventions several times until the researchers make certain that given interventions was successfully mastered in each of the first and second sessions.

◆ **Third session** was done for reinforcement and answer to any patients' questions.

IV. Evaluation phase: All patients were reassessed immediately, 4 weeks, then 8 weeks post implementation of the educational program using the study tools to evaluate the impact of the educational program. The time consumed for each patient's evaluation was about 20-30 minutes.

8.Statistical analysis:

After data were collected and transferred into specially designed formats, so as to be suitable for computer feeding. Data were analyzed using computer with statistical package for social sciences (SPSS) version 18. Complete confidentiality was maintained while the data were being processed.

9.Data analysis:

The following statistical measures were used:

- Descriptive statistics including frequency, distribution, mean, and standard deviation were used to describe different characteristics.
- Kolmogorov – Smirnov test was used to examine the normality of data distribution.
- Univariate analyses including: Friedman test was used to test the significance of results of quantitative variables. Chi-Square test was used to test the significance of results of qualitative variables.
- Linear correlation was conducted to show correlation between score of knowledge

with scores of severities of side effects and self-care practices among the studied patients using Spearman Rho correlation coefficient.

- The significance of the results was at the 5% level of significance.

10. Ethical considerations:

- Written Patient's consent was obtained after explanation of the study aim.
- Confidentiality and privacy were ascertained.
- Patient's right to be withdrawn at any time of research participation was considered and respected.

Results:

The results of the present study were categorized and presented into four main parts as the following:

Part I: Patient's socio-demographic data

Table (1): It shows the distribution of the studied patients with chronic HCV in relation to their socio-demographic data. This table illustrates that half of the studied patients (50%) were in the age group of (50- <60) years. Also, this table revealed that more than half (57.5%) of the studied patients came from rural area, and the majority (87.5%) of them were married. Moreover, it was found that more than two thirds and more than half (70 %, 52.5%) of the subjects did not have sufficient income to fulfill daily requirements of living and have 4-6 children respectively. it was evident that illiterate patients formed more than half (60%) of the subjects and the highest percentage (82.5 %) of them were nonsmokers.

Part II: Differences between patient's knowledge pre, 4- and 8-weeks post implementation of educational nursing interventions program

Table (2): Distribution of the studied patients in relation to their knowledge about chronic HCV at 3 intervals; pre, 4-, and 8-weeks post implementation of educational nursing intervention program. This table clarifies that all of the knowledge scores of the studied patients with chronic HCV related to their disease were highly statically significantly improved 4- and 8-weeks post implementation of the program, since all Ps were < 0.001 except for genotypes of HCV (P= 0.004).

Table (3): Distribution of the studied patients in relation to their knowledge concerning EHMs and their nursing interventions at 3 intervals**;** pre, 4-, and 8-weeks post implementation of the educational program. This table shows that all of the knowledge scores of the studied patients with chronic hepatitis C related to EHMs, and their nursing interventions were highly statically significantly improved after applying the educational program, since all Ps were < 0.001.

Part III: Differences between severities of EHMs that affecting life style experienced by patients pre and post implementation of the educational program

Table (4): Distribution of the studied patients with chronic HCV in relation to fatigue and outcomes of educated nursing interventions at 3 different intervals; pre, 4, and 8 weeks post implementation of educational program as experienced by the patients.

The results reflected that (42.5%, 47.5%, and 57.5%) of the studied patients experienced fatigue pre, 4 weeks, and 8 weeks post implementation of educational program respectively without statistically significant difference between pre and post implementation of educational program on the subjects (p =0.393).

Regarding to severity of fatigue as experienced by the studied patients (17.5%, 15%, 10%) while (22.5%, 12.5%, 12.5%), and (25%, 27.5%, 5.0%) of the studied patients suffered from severe, moderate and mild fatigue pre, 4-, and 8-weeks post implementation of teaching unit respectively without statistically significant difference between pre and post implementation (^{MC}P=0.488).

The table also illustrates that the highest percentage (29.4%) of the studied patients performed day rest, night sleep and the lowest percentage (5.9%) took night warm bath. Furthermore, two thirds (69.9%) of the subjects performed day rest and take more water or fluids while the lowest percentage (4.3%) of them used night sleep, analgesics and avoid fatty food and (17.4%) of them received warm night fluids 8 weeks post implementation of educational program.

Regarding the effect of educated nursing interventions, the results revealed that (70.6%) of the studied patients reported partial relief of fatigue pre implementation of educational program compared to (78.9%) of them reported it 4 weeks post implementation of educational program. while all (100%) of the studied patients reported partial relief of fatigue 8 weeks post educational program without statistically significant difference (p=0.051).

Table (5) represents that more than one third (42.5%) of the subjects suffered from myalgia or joint pain pre implementation of educational program while nearly half (47.5%) of them reported this symptom 4weeks post implementation of educational program and nearly one third (32.5%) of the studied patients reported myalgia or joint pain 8 weeks post implementation of educational program.

Furthermore, the **effect of educated nursing interventions**, the finding showed that nearly two thirds (64.7%) of the subjects reported partial relief of myalgia or joint pain pre implementation of educational program respectively. In addition, (63.2%) of them 4 weeks post implementation of educational program compared to (100%) of them 8 weeks post implementation of educational program reported partial relief of myalgia or joint pain without significant difference between pre post implementing educational program on the subjects (p=0.086).

Table (6) shows that (20%, 17.5%, and 2.5%) of the studied patients experienced depression pre implementation of educational program and 4- and 8-weeks post implementation of educational program respectively.

Regarding the severity of depression, the findings reflected that (5%, 15%) of the patients pre educational program compared to ((10%, 5%) of them 4 weeks post its implementation reported depression as moderate and quite a bit or severe respectively. Moreover (2.5%) of them 8 weeks post implementation of educational program reported it as moderate. The difference between pre and post implementing educational program on the studied patients was not statistically significant (^{LRP}=0.279).

Concerning the educated nursing interventions, pre implementation of teaching unit (37.5 %) of the studied patients performed combination of nursing interventions which include listening to Quran, praying, and going open area while (12.5%) of them made good things in general, wash for praying and tell El-Zaker. The table also revealed that more than half (57.1%) of them performed praying while (14.3%) of them performed combination of nursing interventions that involve reading or watching TV, Al-Zeker, and other practices as sleep or isolation 4 weeks post implementation of educational program.

As regards the effect of educated nursing interventions, (25%) of patients pre educational program compared to (14.3%) of them 4 weeks post its implementation reported complete relief. The difference between pre, post implementation of educational program on the studied patients was not statistically significant (P=0.775).

Part VI: Correlations between patient's knowledge scores, educated nursing interventions and severity of EHMs

Table (7): Knowledge scores about chronic HCV among the studied patients pre and post implementation of educational program. This table illustrates that there is a highly statistically significant difference between the studied patients' knowledge scores about HCV infection, EHMs and educated nursing interventions pre educational program and 4- and 8-weeks post it implementation (P<0.0001*). Generally, there is a highly significant difference between the studied patients' total knowledge scores pre implementation educational program and 4- and 8-weeks post implementation of educational program (P<0.0001*).

Table (8): Severity of EHMs that affecting life style scores among the studied patients pre and post implementation of educational program. The table shows that there is no significant difference between the scores of severities of side effects among the studied patients pre educational program and 4- and 8-weeks post its implementation (P=0.991).

Table (9): Scores of educated nursing interventions among the studied patients pre and post implementation of educational program. The table represents that there is no significant difference between the scores of educated nursing interventions of among the studied patients pre implementation of educational program and 4- and 8-weeks post implementation of educational program (P=0.991).

Table (10): Correlation between knowledge, severity of EHMs and educated nursing interventions scores among the studied patients. This table shows that there is no significant difference between scores of knowledges with scores of severities of manifestations pre educational program and 4 weeks post its implementation (p=0.769,0.136). The table also revealed that there is significant difference between knowledge and educated nursing interventions scores pre implementation of educational program (p=0.01)

Table (11): Correlation between of manifestations scores and educated nursing interventions scores among the studied patients. The table illustrates that there is no significant difference between scores of educated nursing interventions with scores of severities of manifestations pre and 4 weeks post implementation of educational program (p=0.106,0.354). While there is significant difference between them 8 weeks post implementation of educational program (p=0.023).

Table (1): The distribution of the studied patients with chronic HCV in relation to their socio-demographic data.

Socio-demographic characteristics	Studied patients(n=40) No.	%
Age (years)		
20-	3	7.5
30-	6	15.0
40-	11	27.5
50-<60	20	50.0
Place of Residence		
Rural	23	57.5
Urban	17	42.5
Marital status		
Married	35	87.5
Single /Divorced/widow	5	12.5
Level of Education		
Illiterate	24	60.0
Read and write/ Basic education	7	17.5
Secondary education	7	17.5
University or higher	2	5.0
occupation		
Manual	14	35.0
Professional	21	52.5
Housewife	5	12.5
Family income		
Not enough	28	70.0
Enough	12	30.0
No of children		
No	2	5.0
1-3	16	40.0
4-6	21	52.5
More than 6	1	2.5
Smoking habit		
Non-smoker	33	82.5
Smoker	7	17.5
Cigarette smokers	6	15.0
Shisha smokers	1	2.5
Number of cigarettes smoked daily [n=6]		
1 pack or less	5	83.3
3 packs or more	1	16.7

Table (2): Knowledge of the studied patients regarding HCV infection at 3 different intervals pre, 4-, and 8-weeks post implementation of educational nursing intervention program.

Knowledge		Studied patients (n=40)						Chi- Square test
		Pre implementation of educational program		4 weeks Post implementation of educational program		8 weeks Post implementation of educational program		
		No.	%	No.	%	No.	%	
Knowledge about HCV infection	**score**							
Nature of HCV infection	Good	0	0.0	33	82.5	36	90.0	P<0.0001*
	Fair	3	7.5	1	2.5	3	7.5	
	Poor	37	92.5	6	15.0	1	2.5	
Genotypes of HCV	Good	0	0.0	1	2.5	6	15.0	P=0.004*
	Fair	0	0.0	3	7.5	5	12.5	
	Poor	40	100.0	36	90.0	29	72.5	
Signs and symptoms of HCV	Good	0	0.0	6	15.0	9	22.5	P<0.0001*
	Fair	9	22.5	31	77.5	31	77.5	
	Poor	31	77.5	3	7.5	0	0.0	
Risk factors of HCV infection	Good	0	0.0	2	5.0	0	0.0	P<0.0001*
	Fair	13	32.5	37	92.5	40	100.0	
	Poor	27	67.5	1	2.5	0	0.0	
Modes of HCV transmission	Good	0	0.0	21	52.5	21	52.5	P<0.0001*
	Fair	7	17.5	16	40.0	18	45.0	
	Poor	33	82.5	3	7.5	1	2.5	
Diagnosis of HCV	Good	0	0.0	7	17.5	6	15.0	P<0.0001*
	Fair	9	22.5	29	72.5	33	82.5	
	Poor	31	77.5	4	10.0	1	2.5	
Complications of HCV	Good	0	0.0	0	0.0	1	2.5	P<0.0001*
	Fair	6	15.0	30	75.0	33	82.5	
	Poor	34	85.0	10	25.0	6	15.0	

***Significant at P≤0.05**

Table (3): Distribution of the studied patients in relation to their knowledge about EHMs that affecting life style and nursing interventions to manage them at 3 intervals; pre, 4-, and 8-weeks post implementation of the educational program.

Knowledge about EHMs and their nursing interventions		Studied patients (n=40)						Chi-Square test
		Pre educational program		After 4 weeks		After 8 weeks		
		No.	%	No.	%	No.	%	
Are there any EHMs that may be result from chronic hepatitis c?	No /not know	35	87.5	0	0.0	0	0.0	P<0.0001*
	Yes	5	12.5	40	100.0	40	100.0	
What are them?	Poor	35	87.5	2	5.0	1	2.5	
	Fair	5	12.5	38	95.0	39	97.5	
	Good	0	0.0	0	7.5	0	0.0	
Nursing interventions	Poor	40	100.0	3	0.0	2	5.0	
	Fair	0	0.0	37	92.5	38	95.0	
	Good	0	00	0.0	0.0	0.0	0.0	P<0.0001*

***Significant at P≤0.05**

Table (4): Distribution of the studied patients with chronic HCV in relation to fatigue and outcomes of educated nursing interventions at 3 different intervals; pre, 4-, and 8-weeks post implementation of educational program as experienced by the patients.

Extra hepatic manifestations affecting life style		Studied patients (n=40)						Chi- square test
		Pre implementation of educational program		4 weeks Post implementation of educational program		8 weeks Post implantation of educational program		
		No.	%	No.	%	No.	%	
Fatigue	Absent	23	57.5	21	52.5	17	42.5	
	Present	17	42.5	19	47.5	23	57.5	P=0.393
Severity	Mild	4	10.0	5	12.5	2	5.0	MCP=0.488
	Moderate	6	15.0	5	12.5	11	27.5	
	Severe	7	17.5	9	22.5	10	25.0	
Nursing interventions	None	3	17.6	1	5.3	0	0.0	
	Day rest	5	29.4	12	63.2	16	69.6	
	Night sleep	5	29.4	2	10.5	1	4.3	
	Ventilation	0	0.0	0	0.0	2	8.7	
	More water/fluids	2	11.8	9	47.4	16	69.6	
	Walking	0	0.0	6	31.6	3	13.0	
	Avoid exertion	0	0.0	2	10.5	0	0.0	
	Avoid fatty food	0	0.0	1	5.3	1	4.3	
	Warm night bath	1	5.9	8	42.1	4	17.4	
	Analgesics	3	17.6	1	5.3	1	4.3	
	Others (Massage, cold shower, sleep)	0	0.0	1	5.3	2	8.7	
Effectiveness of nursing interventions on decreasing the severity of fatigue	Not used	3	17.6	1	5.3	0	0.0	
	no relief	2	11.8	1	5.3	0	0.0	
	Partial relief	12	70.6	15	78.9	23	100.0	P=0.051
	Complete relief	0	0.0	2	10.5	0	0.0	

Table (5): Distribution of the studied patients with chronic HCV according to Myalgia/ joint pain and outcomes of educated nursing interventions at 3 different intervals; pre, 4-, and 8-weeks post implementation of educational program as experienced by the patients.

Extra hepatic affecting life style	manifestations	Studied patients (n=40) Pre implementation of educational program		4 weeks Post implementation of educational program		8 weeks Post implementation of educational program		Chi-Square test
		No.	%	No.	%	No.	%	
Mylagia/ joint pain	Absent	23	57.5	21	52.5	27	67.5	
	Present	17	42.5	19	47.5	13	32.5	P=0.381
Severity	Not at all/ A little	3	7.5	8	20.0	0	0.0	^{MC}P=0.005*
	Moderate	8	20.0	4	10.0	4	10.0	
	Quite a bit / V. severe	6	15.0	7	17.5	9	22.5	
Nursing Interventions	None	5	29.4	3	15.8	0	0.0	
	Exercises	0	0.0	3	15.8	2	15.4	
	Massage	2	11.8	7	36.8	8	61.5	
	Local creams	6	35.3	4	21.1	5	38.5	
	Rest	5	29.4	3	15.8	2	15.4	
	Others (icepacks, compressive bandage, warm compresses or shower)	1	5.9	5	26.3	11	84.6	
Effectiveness of nursing interventions on decreasing the severity of myalgia/joint pain	Not used	5	29.4	3	15.8	0	0.0	P=0.086
	no relief	1	5.9	1	5.3	0	0.0	
	Partial relief	11	64.7	12	63.2	13	100.0	
	Complete relief	0	0.0	3	15.8	0	0.0	

Table (6): Distribution of the studied patients with chronic HCV according to depression and effectiveness of educated nursing interventions at 3 different intervals; pre, 4, 8 weeks post implementation of educational program as experienced by the patients.

Extra hepatic manifestations affecting life style		Studied patients (n=40)						Chi-Square test
		Pre implementation of teaching unit		4 weeks post implementation of teaching unit		8 weeks post implementation of teaching unit		
		No.	%	No.	%	No.	%	
Depression	Absent	32	80.0	33	82.5	39	97.5	
	Present	8	20.0	7	17.5	1	2.5	**P=0.045***
Severity	Not at all/ A little	0	0.0	1	2.5	0	0.0	
	Moderate	2	5.0	4	10.0	1	2.5	LRP=0.279
	Quite a bit/ V. severe	6	15.0	2	5.0	0	0.0	
Educated nursing interventions	None	0	0.0	0	0.0	0	0.0	
	Hear Quran	3	37.5	3	42.9	0	0.0	
	Reading/TV	0	0.0	1	14.3	0	0.0	
	Light exercise	0	0.0	2	28.6	0	0.0	
	Open areas	3	37.5	0	0.0	1	100.0	
	Praying	3	37.5	4	57.1	0	0.0	
	Wash for praying	1	12.5	3	42.9	0	0.0	
	Visit relatives / friends	0	0.0	0	0.0	1	100.0	
	Al-Zekr	1	12.5	1	14.3	0	0.0	
	Make good things generally	1	12.5	1	14.3	0	0.0	
	Others	0	0.0	1	14.3	0	0.0	
Effect of educated nursing interventions	Not used	1	12.5	0	0.0	0	0.0	
	Partial relief	5	62.5	6	85.7	1	100.0	
	Complete relief	2	25.0	1	14.3	0	0.0	P=0.775

Table (7): Knowledge scores about HCV among the studied patients pre and post implementation of educational program.

Knowledge items	Knowledge Score						Friedman test
	Min-Max	Mean±SD	Poor (< 50%)		Good (>70%)		
			No.	%	No.	%	
About chronic HCV							
• Pre implementation of educational program	0.0-35.7	8.4±10.7	40	100.0	0	0.0	P<0.0001*
• 4 weeks post implementation of educational program	14.3-74.4	51.2±13.4	31	77.5	9	22.5	
• 8 weeks post implementation of educational program	28.6-78.6	57.3±11.4	22	55.0	18	45.0	
About treatment							
• Pre implementation of educational program	0.0-68.8	10.2±18.7	38	95.0	2	5.0	P<0.0001*
• 4 weeks post implementation of educational program	12.5-81.3	59.4±14.8	14	35.0	26	65.0	
• 8 weeks post implementation of educational program	43.8-81.3	60.3±8.6	19	47.5	21	52.5	
About EHMs							
• Pre implementation of educational program	0.0-25.0	3.1±8.4	40	100.0	0	0.0	P<0.0001*
• 4 weeks post implementation of educational program	0.0-50.0	46.9±11.6	40	100.0	0	0.0	
• 8 weeks post implementation of educational program	25.0-50.0	48.1±6.7	40	100.0	0	0.0	
Total score							
• Pre implementation of educational program	0.0-44.1	8.6±13.1	40	100.0	0	0.0	P<0.0001*
• 4 weeks post implementation of educational program	14.7-67.6	54.6±11.5	29	72.5	11	27.5	
• 8 weeks post implementation of educational program	35.3-73.5	57.6±7.4	24	60.0	16	40.0	

***Significant at P≤0.05**

Table (8): Severity of EHMs that affecting life style scores among the studied patients pre and post implementation of educational program

Severity of side effects	n	Scores Min-Max	Mean±SD	Low (<50%) No.	%	High (>70%) No.	%	Friedman test
• Pre implementation of educational program	32	20.0-100.0	60.9±16.4	11	34.4	21	65.6	P=0.991
• 4 weeks post implementation of educational program	37	20.0-100.0	60.8±17.8	17	45.9	20	54.7	
• 8 weeks post implementation of educational program	40	20.0-93.3	60.5±17.3	18	45.0	22	55.0	

Table (9): Scores of educated nursing interventions among the studied patients pre and post implementation of educational program

Educated nursing interventions	n	Score Min-Max	Mean±SD	Low (<50%) No.	%	High (>70%) No.	%	Friedman test
• Pre implementation of educational program	32	0.0-100.0	46.0±27.8	12	37.5	20	62.5	P=0.991
• 4 weeks post implementation of educational program	37	0.0-83.3	46.5±24.5	12	32.4	25	67.6	
• 8 weeks post implementation of educational program	40	0.0-83.3	53.5±17.5	17	42.5	23	57.5	

Table (10): Correlation between knowledge, scores about severity of manifestations and educated nursing interventions scores among the studied patients

Scores	Knowledge Score Pre educational program r	P	4 weeks post educational program r	P	8weeks post educational program r	P
Severity of manifestations	0.054	0.769	0.25	0.136	**-0.5**	**0.001***
Nursing interventions score	**0.447**	**0.01***	0.162	0.337	0.048	0.7 69

r: Spearman Rho correlation coefficient *significant at P≤0.05

Table (11): Correlation between of manifestations scores and educated nursing interventions scores among the studied patients

	Scores of educated nursing interventions					
	Pre implementation of educational program		4 weeks post implementation of educational program		8weeks post implementation of educational program	
	r	P	r	P	r	P
Score of manifestations	0.291	0.106	0.157	0.354	**0.359**	**0.023***

r: Spearman Rho correlation coefficient *significant at P≤0.05

Discussion

Chronic hepatitis C virus infection affect 71 million people worldwide. HCV is hepatotropic virus, is known for morbidity due to its liver complications (cirrhosis and hepatocellular carcinoma), with an estimated 350,000 liver-related deaths per year. Among all viruses, hepatotropic and non-hepatotropic, HCV is recognized as the virus most often associated with EHMs. Extrahepatic manifestations involve many organs and tissues of the body **Cacoub, & Saadoun, (2021).**

The current study clarifies that all of the knowledge scores of the studied patients with chronic HCV related to their disease, EHMs and their nursing interventions were highly statically significantly improved after implementation of the nursing intervention program This might be attributed to the theoretical sessions that were provided to cover all aspects of hepatitis C virus which eventually increase patient's knowledge. Increased HCV-related knowledge was associated with greater perceptions of HCV. This result is in line with **Chawla, et al, (2019); Saine, et al,(2019)** who reported that effective health education consequently improves knowledge of patients and their perception. While it was contradicted by Ibrahim 2012 who illustrated that there was no significant difference in knowledge score between patients who received information about their disease and therapy from specialized physicians and others and all the knowledge score was low.

Regarding fatigue; the results reflected that around half of the studied patients experienced fatigue pre, 4 weeks, and 8 weeks post implementation of educational nursing program which confirmed that fatigue is a symptom of HCV infection. This finding is in line with **Fagundes, Ferreira, & Lima Pace, (2020; Pomper (2014)** who mentioned that the most frequent complaint of HCV patients is fatigue.

Although increased number of the studied patients with severe level of fatigue after implementation of educational program than before, all of the studied patients reported partial relief of fatigue after implementation. This result may be related to the effect of the program on the severity of EHMs. This result was coordinated with **Mohsen (2011)** who found that fatigue was decreased among the study group subjects than control group after giving the nursing intervention.

In relation to arthralgia/myalgia: Arthralgia is reported in 40-80 % of HCV-infected patients, affecting mainly knees and hands with bilateral and symmetric pain as mentioned by **Kuna, Jakab, Smolic, Y Wu, & Smolic, (2019).** This contradicted with the current finding which clarifies that more than one third (42.5%) of the subjects suffered from myalgia or joint pain pre implementation of educational. This may be related to small number of samples. Also**, Su, et al, (2014)** reported that Rheumatologic involvement is the most frequent extra-hepatic manifestation of HCV.

Although the severity of myalgia or arthralgia did not decrease after the implementation of the program, all of the studied patients reported partial relief of them post implementation of the program, it may be related to effect of implementation of educational program. Nursing intervention provide partial relief of patients' symptoms which confirm its need to be combined with pharmacological drugs and continuity of care. Furthermore, the educated nursing interventions to be more effective need to be life style rules which practice all over the life. This result of the current study was in line with **Sung et al, (2011)** mentioned that certain interventions such as maintaining adequate hydration and light to moderate exercise keep patients tend to feel better. While it contradicted with the results of **Mohsen, (2011)** who found that there was highly significance difference of patients complain before the study and after 4 and 8 weeks.

Concerning depression; Although the findings of current study explored that there wasn't significantly decrease in the severity of depression, the number of the studied patients who had depression and severity of it post the implementation of educational program were more decreased than pre implementation of it. Additionally, the results revealed that the percentages of the studied patients who report partial relief were increased post implementation of educational program than its pre implementation. These might be return to the effect of performing combination of educated nursing interventions during program. Furthermore, most of these measures are religious beliefs which identified and performed by most of patients naturally.

These results were in line with **Cinar, Ozdogan. & Alahdab, (2015)** who stated that Pre-education depression scores were higher than post education depression scores. Specific educational programs provided by nurses improved patients' quality of life and decreased depression among HCV patients. Also, **Badrakalimuthu, Rumball. & Chaw, (2011)** mentioned that patient education, restorative therapy, comprising exercise and behavioral programs, can address cognitive alterations and improve mood state, functional capacity and activity tolerance.

Stress reduction techniques can play a main role in depression reduction and development of social adaptability through modifying inappropriate social information-processing patterns **Song, & Lindquist, (2015); Abbasian, Najimi, Meftagh, Ghasemi, & Afshar, (2014).** Additionally, Support group can offer a safe space to discuss the emotional issues surrounding HCV and its treatment this mentioned by **Franciscus, and Highleyman, (2011).** Furthermore, patients should get support from their family and friends, practice positive thinking, find ways to laugh and amuse themselves, and to try to be physically active a little bit every day and avoid isolation. Furthermore, USA Department of **Veteranse Affairs, (2015)** stated that Simple self-care practices such as going to sleep, waking up at the same time every day, reading or watching TV before bed, limiting daytime naps, avoiding caffeinated products, especially in the afternoon and at night, and may be recommended to relieve insomnia.

The findings show that there is no significant difference between the scores of knowledge, severity and educated nursing interventions of extrahepatic manifestations among the studied patients pre implementation of the program and 4- and 8-weeks post its implementation. This may be attributed by impaired memory and concentration of the studied patients, noisy environment of hospital, patients prefer interventions that had rapid effect and this not available in many nursing interventions or beliefs of some patients that these interventions are not effective and sufficient to relieve their symptoms. This might also be attributable to the large percentage of the studied patients were from rural areas with less devotion to gaining of knowledge due to more than half of them were illiterate. These results were contradicted with **Mohsen**, **Fareed, El-Sheikh, & Abbas, (2011)** who illustrate that their study revealed that

enrichment of patients with nursing intervention and knowledge about chronic hepatitis C, seemed to have positive effects on improving patients' knowledge about diseases and managing their symptoms and self-care modalities that reflected by improvement of patients complains especially fatigue level.

Finally, the results show that number of patients suffering from manifestations were increased during period of the study; this may be related to over activity, stress, some medications, environmental factors or progression of disease.

Conclusion and recommendations:

In conclusion, although this study illustrated that all of the knowledge scores of the studied patients with hepatitis C virus related to chronic HCV infection, , its extrahepatic manifestations and nursing interventions to deal with these manifestations were highly statistically significant improved post implementation of the educational program, there is no significant difference between the scores of severity of extrahepatic manifestations among the studied patients pre and post implementation of educational program. Additionally, there were no significant differences between score of nursing interventions with scores of severities of extrahepatic manifestations pre and 4 weeks post implementation of the program. While there were significant differences between them 8 weeks post implementation of educational nursing intervention.

It is recommended that, the educational nursing program should be applied to all patients in suitable environment for teaching and supported with more audiovisual materials. Furthermore, reinforcement sessions should be continued during patients follow up in outpatients' clinics.

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