Original Article

DOI: 10.4274/haseki.galenos.2024.9910
Med Bull Haseki 2024;62:280-286

Frequency of Fibromyalgia in Patients with Chronic Hepatitis C Virus Infection and Its Relationship with Vitamin D Levels and Quality of Life

Havva Talay Calis*, Fatma Gul Ulku Demir**, Ulas Serkan Topaloglu***, Hatice Sayan****, Deniz Kamalak Guzel*****, Emel Guler******, Fatma Samli*******, Caglar Karabas********, Serap Tomruk Sutbeyaz*, Hatice Kayis Topaloglu*********

*University of Health Sciences Turkey, Kayseri Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Kayseri, Turkey

**Kayseri City Education and Research Hospital, Clinic of Physical Medicine and Rehabilitation, Kayseri, Turkey

***Kayseri City Education and Research Hospital, Clinic of Internal Medicine, Kayseri, Turkey

****University of Health Sciences Turkey, Mehmet Akif Inan Training and Research Hospital, Clinic of Physical Medicine and Rehabilitation, Sanliurfa, Turkey

*****Kayseri City Education and Research Hospital, Clinic of Infectious Diseases, Kayseri, Turkey

******Gazi University Faculty of Medicine, Department of Anaesthesiology and Reanimation, Division of Pain Medicine, Ankara, Turkey

*******University of Health Sciences Turkey, Ankara Gaziler Physical Therapy and Rehabilitation Training and Research Hospital, Clinic of Physical Medicine and Rehabilitation, Ankara, Turkey

********Private Clinic, Department of Physical Medicine and Rehabilitation, Antalya, Turkey

*********Turgut Reis Family Health Center, Department of Family Medicine, Kayseri, Turkey

Abstract

Aim: The literature on the effects of the fibromyalgia syndrome (FMS) association with hepatitis C virus (HCV) on quality of life and vitamin D levels is limited. We aimed to evaluate the frequency of fibromyalgia in patients with chronic hepatitis C virus (HCV) and also to analyze the relationship between the presence of fibromyalgia and vitamin D parameters.

Methods: This controlled, cross-sectional study of 123 participants (72 patients with HCV and 51 in the control group) was conducted in a tertiary hospital. The study enrolled age- gender and BMI-matched control groups. Patients were diagnosed with fibromyalgia and arthritis as per the 2010 American College of Rheumatology diagnostic criteria. Fibromyalgia Impact Questionnaire (FIQ), Nottingham Health Profile (NHP) and the level of vitamin D were performed in all patients.

Results: The presence of fibromyalgia, the level of vitamin D and the score of FIQ were statistically different between HCV (+) and control groups. The score of social isolation was higher in the HCV (+) group, whereas all other scores were similar in both groups according to the NHP scale. Based on the presence or absence of fibromyalgia, all scores of FIQ and NHP scales were higher in a subgroup with fibromyalgia. This study documented a prevalence of 56.9% of FMS in patients with HCV (+) in comparison to the control group

Conclusion: This study documented a high prevalence of 56.9% of FMS in patients with HCV (+) in comparison to the control group. While emphasizing raising awareness of fibromyalgia, its relationship with HCV, vitamin D, quality of life, age, gender, BMI, and tender points was revealed via regression analysis.

Keywords: Fibromyalgia, hepatitis C virus, vitamin D, quality of life

Address for Correspondence: Fatma Gul Ulku Demir, Kayseri City Hospital, Clinic of Physical Medicine and Rehabilitation, Kayseri, Turkey
E-mail: mdfgudemir@gmail.com **ORCID:** orcid.org/0000-0003-4160-8568
Received: 08.05.2024 **Accepted:** 17.12.2024

Introduction

Fibromyalgia syndrome (FMS) is characterized by diffuse musculoskeletal pain, fatigue, and sleep disorders that negatively affect quality of life (1). Chronic hepatitis C virus infection (HCV) is one of society's most common viral infections. HCV plays a role in the pathogenesis of autoimmune, rheumatological, and musculoskeletal diseases (2). Chronic viral infections trigger FMS symptoms through inflammatory mediators, cytokines, and low IGF-1 levels (3). Studies have found that the prevalence of FMS in patients with HCV infection is 1.9-57% (4). However, these studies focused on tender points in the FMS diagnostic criteria. After the FMS diagnostic criteria were changed in 2010, tender point examination was removed from the FMS diagnostic criteria. Symptoms are mainly diagnosed according to the widespread pain index (WPI) and symptom severity (SS). A prevalence study should be conducted according to these new criteria.

The prevalence of vitamin D deficiency ranges from 46% to 92% in chronic HCV infection population screening (3,5). A study examining vitamin D's effect on liver fibrosis reported that low vitamin D levels were observed in 80%. Vitamin D deficiency is also linked to liver fibrosis and cirrhosis progression (5). Vitamin D levels have also been shown to decrease in chronic diseases, and this relationship has been documented in increasingly different studies on a daily basis (6). Vitamin D deficiency, which affects quality of life, is frequently observed in chronic diseases and adds synergy to people's suffering and considerably reduces their quality of life (3,6). While vitamin D maintains normal bone mineralization by affecting the absorption of minerals such as calcium from the intestine, it is a powerful biomodulator that affects cell metabolism and differentiation as a powerful biomodulator with vitamin D receptor activation (7).

Serum vitamin D levels were significantly lower in patients with FMS than in the control group. Vitamin D deficiency contributes to the progression of chronic hepatitis in HCV. Low vitamin D levels are associated with fibrosis in HCV. Low vitamin D levels can cause muscle weakness and sarcopenia (8). Studies have reported high vitamin D deficiency rates in patients with chronic liver disease. However, the literature on the effects of the FMS association with HCV on quality of life and vitamin D levels is limited (9).

We aimed to evaluate the frequency of FMS in patients with HCV according to the 2010 diagnostic criteria and to analyze the relationship between FMS and vitamin D deficiency and quality of life.

Materials and Methods

Compliance with Ethical Standards

A local university ethics committee approved our study protocol, and approval was received from the Erciyes University Ethical Committee before starting the study (date: 16.06.2017, decision number: 2017/330). All participants provided written informed consent, and the study was conducted in accordance with the Human Rights Declaration.

Study Design

A controlled, cross-sectional study. People 18-65 were admitted to the Physical Therapy and Rehabilitation outpatient clinic of Kayseri City Education and Research Hospital in Turkey between July 2019 and January 2020. A total of 123 patients (98 female, 25 male) were included in the study, of whom 72 (58 female, 14 male) patients were classified into the hepatitis C virus (+) group, and 51 (40 female, 11 male) patients were classified into the HCV (-) control group.

Patients with positive HCV-RNA and liver biopsy results in the infectious diseases outpatient clinic were included in the study. Those with newly diagnosed acute hepatitis C infection, any hepatitis other than HCV, end-stage liver cirrhosis, uncontrolled systemic disease (another bacterial or viral infection, congestive heart failure, renal failure, epilepsy, organ transplantation), congenital or acquired physical deformities (kyphoscoliosis, scoliosis, agenesis, amputation), the affected musculoskeletal system due to neurological diseases (stroke, muscular dystrophy, Guillain-Barre), pregnant and lactating patients, or a history of trauma in the last week were not included. Patients who met the inclusion criteria were referred to the Physical Medicine and Rehabilitation (PMR) outpatient clinic and included in the study.

HCV (-) patients who applied to the PMR outpatient clinic for any reason (due to waist, neck, shoulder, hip, knee, ankle, or joint pain) who met the exclusion criteria of this study were included in the control group. Age, gender, and body mass index (BMI)-matched control group participants were enrolled in the study.

HCV was diagnosed in patients with antibodies against HCV (anti-HCV) and serum HCV ribonucleic acid (RNA). Detailed rheumatological and neurological examinations were performed to differentially diagnose the patients. A specialist physician in physical medicine and rehabilitation diagnosed patients with FMS according to the 2010 American College of Rheumatology (ACR) diagnostic criteria (10).

Interventions

Patients' age, gender, height, weight, HCV disease duration, 2010 diagnostic criteria, FIQ, and NHP scores were questioned. A fasting venous blood sample was collected after an overnight fast of at least 8 h for biochemical investigations, and samples were processed at the hospital laboratory on the same day. The Chroma Systems Kit on the Agilent 1200 device was used with

HPLC in 0.5 mL of plasma taken into a tube with EDTA and 25 (OH) vitamin D levels were studied. Regarding 25 (OH) D vitamin status, those below 20 ng/mL were considered vitamin D deficient, those between 21-29 ng/mL, vitamin D insufficient, and those above 30 ng/mL, with sufficient vitamin D levels. The HCV (+) and HCV (-) control groups were compared for all these parameters. In addition, as a subgroup analysis in the HCV (+) group, patients with and without FMS were compared for the same parameters.

Diagnosis of FMS

According to ACR 2010 diagnostic criteria, the WPI and SS scale were used (10). The WPI shows the number of areas where the patient has experienced pain in the past week. Each region in which pain is felt gets 1 point. Score ranges from 0 to 19. In the SS scale, the severity of 1) fatigue, 2) waking up tired in the morning, 3) cognitive symptoms, and 4) somatic symptoms in the last week were assessed. These four items were scored between 0 and 3 (0=normal, 1=mild, 2=moderate, and 3=severe). The total score ranges from 0 to 12. For diagnosis of FMS, the WPI must be seven or more and SS 5 or more, or the WPI must be 3-6 and SS 9 or more. The symptoms should have been ongoing for at least three months, and there should be no other disease to explain the pain.

The Fibromyalgia Impact Questionnaire

The Fibromyalgia Impact Questionnaire (FIQ), whose Turkish validity was performed by Sarmer et al. (11), calculated patients' functional status and disease progression. The first item of the scale comprises 10 Likert-type questions. Participants were asked to select the days to determine "absence from job" and "exposure to disease" in the second and third items. The scores provided are adapted to ten. The seven questions are also based on selecting the corresponding points on an equivalent visual scale. The score interval is 0-100; a higher score indicates a higher level of physical disability.

The Nottingham Health Profile

The Nottingham Health Profile (NHP) is a self-reported questionnaire that measures perceived health status. According to a Turkish validation study of the NHP, it is a reliable and validated psychometric scale, which includes 38 questions (answered yes/no) that form six statements of distress: pain (eight items), physical mobility (eight items), energy (three items), sleep (five items), social isolation (five items), and emotional reactions (nine items). The item scores were used to calculate the final index of distress. "0 points" indicates no restrictions, and "100 points" indicates the presence of all listed restrictions (12).

Statistical Analysis

The SPSS 22.0 (IBM Corp., Armonk, United States of America) software was used for statistical analysis. Frequencies are expressed as percentages. The chi-square test was used to compare categorical data. The Shapiro-Wilk test and histogram graphs determine whether numeric (digital) data are distributed normally or not. Numeric (digital) data relating to independent groups with a normal distribution were compared using Levene's test and independent samples t-test. Variables with normal distribution are expressed in mean ± standard deviation. If the distribution is abnormal, the Mann-Whitney U test is used. Variables with abnormal distribution are expressed as median (1^{st}-3^{th} quartile). $P<0.05$ is accepted and considered statistically significant.

Results

There were no statistically significant differences between the HCV+ and control groups in terms of gender, age, BMI, vitamin D status (normal, deficiency, insufficiency), and vitamin D ($p>0.05$). Both groups were also compared regarding FMS, vitamin D levels, FIQ, and NHP according to the 2010 criteria (Table 1). When those with and without FMS were compared as a sub-analysis in the HCV (+) group, there was again no statistically significant difference in terms of gender, age, BMI, symptom duration, vitamin D levels, and status ($p>0.05$). FIQ and NHP scores were significantly different (Table 2).

The group's mean age with hepatitis C virus (+) was 58.38±8.2 years, whereas that of the control group was 58.82±9.79 years. The mean body mass index of the group with HCV (+) was 31.98±5.3 kg/m², whereas that of the control group was 30.36±4.31 kg/m². This difference in age, sex, and BMI was insignificant (respectively, $p=0.783$, $p=0.951$, $p=0.075$). The presence of FMS, vitamin D level, and Fibromyalgia Impact Questionnaire score were significantly different between the two groups ($p=0.031$, $p<0.001$, $p=0.004$). The social isolation score was higher in the HCV (+) group. In contrast, scores of pain, physical mobility, energy, sleep, emotional reactions, and total data were similar in both groups, according to the results calculated with the Nottingham Health Profile scale analysis (respectively, $p=0.027$, $p=0.057$, $p=0.959$, $p=0.064$, $p=0.794$, $p=0.129$, $p=0.407$). The results are detailed in Table 1.

Patients with HCV (+) were examined in two subgroups based on the presence or absence of FMS. Age, BMI, disease duration, and vitamin D levels were similar in both subgroups (respectively, $p=0.783$, $p=0.530$, $p=0.915$, $p=0.413$). All subgroup patients with FMS (41 subjects) were female, whereas those without FMS included 17 females and 14 males. All FIQ and NHP scale scores were higher in the FMS subgroup. The results are detailed in Table 2.

Table 1. Clinical data of patients with HCV infection and controls			
	HCV (+) (n=72)	**Control (n=51)**	**p-value**
Sex (F/M), n (%)	58/14 (80.6/19.4)	40/11 (78.4/21.6)	0.951
Age (year), mean ± SD	58.38±8.20	58.82±9.79	0.783
BMI (kg/m²), mean ± SD	31.98±5.30	30.36±4.31	0.075
Fibromyalgia (+/-), n (%)	41/31 (56.9/43.1)	19/32 (37.3/62.7)	**0.031**
Vitamin D (µg/L), median (per 25-75)	11.7 (7.6-20.1)	16.4 (13.0-25.4)	**<0.001**
Vitamin D status, n(%)			
Deficiency	53 (73.6)	28 (54.9)	0.082
Insufficiency	14 (19.4)	15 (29.4)	
Normal	5 (6.9)	8 (15.7)	
FIQ, median (per 25-75)	47.93 (22.9-64.5)	35.66 (14-55)	**0.004**
NHP, median (per 25-75)			
Pain	40.2 (10-78.7)	56.86 (26-100)	0.057
Physical mobility	32.56 (14.5-54.2)	31.29 (21.4-54.5)	0.959
Energy	76 (0-100)	39.2 (0-100)	0.064
Sleep	49.65 (12.6-77.6)	50.37 (12.6-77.6)	0.794
Social isolation	22.01 (0-61.5)	0 (0-42.1)	**0.027**
Emotional reactions	37.97 (9.8-81.5)	23.29 (0-71.8)	0.129
Total	273.4 (133.9-405.1)	240.19 (88.7-353.2)	0.407

P<0.05 considered statistically significant. Depending on normality, the independent samples t-test or Mann-Whitney U test was used
F: Female, M: Male, SD: Standard deviation, BMI: Body mass index, FIQ: Fibromyalgia impact questionnaire, NHP: Nottingham Health Profile

Table 2. Subgroup analysis of patients with HCV infection according to the presence of FMS			
	Fibromyalgia (+) (n=41)	**Fibromyalgia (-) (n=31)**	**p-value**
Sex (F/M), n (%)	41/0 (100/0)	17/14 (54.8/45.2)	-
Age (year), mean ± SD	59.15±8.72	57.35±7.47	0.783
BMI (kg/m²), mean ± SD	32.33±5.52	31.53±5.04	0.530
Duration of symptoms Median (per 25-75)	72 (24-120)	66(24-120)	0.915
Vitamin D (µg/L), median (per 25-75)	11.4 (7.2-19.7)	13.3 (8-20.1)	0.413
Vitamin D status, n (%)			
Deficiency	31 (75.6)	22 (71.0)	0.322
Insufficiency	6 (14.6)	8 (25.8)	
Normal	4 (9.8)	1 (3.2)	
NHP, median (per 25-75)			
Pain	67.35 (36.3-89.5)	9.99 (0-37.5)	**<0.001**
Physical mobility	41.86 (31.3-54.5)	11.54 (0-41.9)	**<0.001**
Energy	100 (69.6-100)	0 (0-100)	**<0.001**
Sleep	77.63 (37.4-77.6)	16.1 (12.6-77.6)	**0.014**
Social isolation	22.53 (22-62.7)	0 (0-42.7)	**0.025**
Emotional reactions	62.58 (22-87)	9.76 (0-56.3)	**0.003**
Total	349.65 (243.6-422.9)	116.38 (38-293.6)	**<0.001**

P<0.05 considered statistically significant. Depending on normality, the independent samples t-test or Mann-Whitney U test was used
F: Female, M: Male, SD: Standard deviation, BMI: Body mass index, NHP: Nottingham Health Profile

Discussion

In this study, according to the 2010 ACR diagnostic criteria, the frequency of FMS was higher in HCV (+) patients than in HCV (-) patients at 56.9%. Vitamin D levels were statistically significantly lower in HCV (+) patients than in HCV (-) individuals. However, when a subgroup analysis of HCV (+) patients was performed, there was no significant difference in vitamin D levels between patients with and without FMS. In HCV (+) patients, the FIQ median and NHP social isolation values. When patients with and without FMS were compared, there was a statistically significant decrease in all NHP scores. Pain, physical mobility, energy, sleep, and emotional reactions, which are fibromyalgia-related factors, were found to be significant for HCV infection.

Our results showed that the frequency of FMS was higher in HCV (+) patients than in HCV (-) patients. In previous studies, the prevalence of FMS in patients with HCV infection ranged from 4% to 57% (13). Our study revealed a significantly higher prevalence rate of 56.9% compared with the control group. Based on our study, which has relatively more recent data than previous studies, it can be concluded that the frequency of FMSs is increasing daily. These results may have been influenced by the high level of scientific awareness, media interest, and the frequently changing definition of FMS, along with psychological disorders. In addition, several conditions, such as socioeconomic factors, demographic data, and genetic differences, may affect FMS. People with HCV infection may have extrahepatic symptoms, such as arthralgia, marked arthritis, painful paresthesias, and peripheral neuropathy, or they may meet the FMS criteria in 25% of cases (13,14). In addition, a recent study mentioned common non-rheumatic medical conditions that mimic FMS, in addition to chronic infections such as HCV (2). These conditions include vitamin B12, C, and D deficiencies; iron and magnesium deficiencies; thyroid dysfunction; obesity; obstructive sleep apnea; neuropathies; chronic infections such as HCV; cancer; and celiac disease; lipid-lowering drugs; bisphosphonates; aromatase inhibitors; and isotretinoin use. However, it may be extremely difficult to distinguish between FMS-like conditions that can be attributed to these conditions and pure FMS (2,13). One of the important limitations of our study is that we did not question all of these factors. Despite this limitation, the fact that vitamin D levels were measured was a strength of our study. The significantly lower vitamin D levels in HCV (+) patients in our study suggest that the prevalence of FMS is increasing. The 2010 FMS diagnostic criteria should also be reconsidered for these conditions.

FMS is a syndrome of unknown cause characterized by chronic widespread musculoskeletal pain lasting more than 3 months, often accompanied by symptoms such as fatigue, non-restorative sleep, cognitive impairment, short-term memory deficit, headache, irritable bowel syndrome, anxiety, and depression (15). FIQ is a scale commonly used in patients with FMS, and its higher detection is considered significant in support of FMS.

Along with increased FMS, the median FIQ score was higher in HCV (+) patients than in HCV (-) ones. The disease duration was longer in patients with FMS in our study, although this difference was not statistically significant (Table 2). We believe that FMS should be added to comorbidities that may occur as the disease duration increases.

Vitamin D deficiency is common among patients with HCV infection and is directly related to disease severity (16). It is also recommended as a supplement to treat HCV infection (3,17). It is also emphasized that vitamin D deficiency plays a role in inflammatory responses via tumor necrosis factor inhibition in chronic liver diseases caused by HCV, and it has been shown that patients with HCV may have a poor prognosis (13,18). According to the findings compatible with the literature we obtained in our study, vitamin D levels should be examined in patients with HCV and replaced if there is a deficiency.

Data on the poor quality of life in patients with chronic hepatitis and cirrhosis are available in previous studies (19,20). Even when HCV (+) people are asymptomatic, significant deterioration in quality of life occurs. In a study conducted by Honrubia-López et al. (21), 86 patients were evaluated using the SF-36 scale, and lower scores were obtained than healthy controls. In another study of patients with chronic viral hepatitis evaluated using the NHP scale, the main areas of worse quality of life were decreased energy, sleep, and emotional reactions (22). Unlike in our study, only the median score of NHP-social isolation was higher in HCV (+) patients than in the control group.

FMS is more common in women (23). Not only compatible with the literature but also surprisingly in our study, there were no male patients among the 41 HCV (+) patients with FMS. As expected, in line with these findings, the median FIQ score was higher in participants with FMS.

Although vitamin D deficiency increases FMS symptoms, FMS patients generally have vitamin D levels similar to those of healthy individuals (20). In this study, vitamin D levels were significantly different in the presence of HCV and not in the presence of FMS. From this, we can conclude that HCV, rather than FMS, affects vitamin D levels.

Generally, all NHP subscale values for patients with FMS are higher than those of the healthy population in studies evaluating the NHP scale (24,25). In our study, patients with HCV (+) were evaluated and divided into

two subgroups according to the presence or absence of FMS. The median scores in all sections of the NHP scale were higher in patients with FMS. Multiple analyses on whether there is FMS or not, only its relationship with NHP-emotional reactions can be revealed.

Study Limitations

We did not intend to determine the effect of HCV transmission route and HCV genotype on FMS symptoms. We included HCV (-) individuals who visited the PMR outpatient clinic for any reason (neck, shoulder, waist, hip, knee pain, joint pain) as the control group. We did not have a control group of completely healthy individuals. Our study's strength lies in its use of the 2010 criteria. It is known that HCV infection alone can affect quality of life. However, we would like to emphasize that the presence of FMS and/or vitamin D deficiency affects the quality of life of HCV. Patients should also be evaluated in this regard.

Conclusion

This study documented a prevalence of 56.9% of FMS in patients with HCV (+) in comparison to the control group. Other painful conditions that resemble fibromyalgia syndrome should also be taken into account. Vitamin D levels were observed to be lower in HCV patients. The quality of life in patients with HCV is primarily limited by social isolation; however, the presence of FMS may further diminish quality of life across various domains, including pain, physical mobility, energy levels, sleep, and emotional responses.

Ethics

Ethics Committee Approval: A local university ethics committee approved our study protocol, and approval was received from the Erciyes University Ethical Committee before starting the study (date: 16.06.2017, decision number: 2017/330).

Informed Consent: All participants provided written informed consent, and the study was conducted in accordance with the Human Rights Declaration.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.T.C., F.G.U.D., U.S.T., H.S., D.K.G., E.G., F.S., C.K., S.T.S., H.K.T., Concept: H.T.C., F.G.U.D., U.S.T., H.S., D.K.G., E.G., C.K., H.K.T., Design: H.T.C., F.G.U.D., H.S., D.K.G., E.G., F.S., C.K., S.T.S., Data Collection or Processing: H.T.C., F.G.U.D., U.S.T., H.S., D.K.G., E.G., F.S., C.K., S.T.S., H.K.T., Analysis or Interpretation: H.T.C., F.G.U.D., U.S.T., D.K.G., E.G., F.S., C.K., S.T.S., H.K.T., Literature Search: H.T.C., U.S.T., H.S., D.K.G., E.G., F.S., C.K., S.T.S., H.K.T., Writing: H.T.C., F.G.U.D., U.S.T., H.S., F.S., C.K., H.K.T.

Conflict of Interest: No conflicts of interest were declared by the authors.

Financial Disclosure: This study received no financial support.

References

1. Jurado-Priego LN, Cueto-Ureña C, Ramírez-Expósito MJ, Martínez-Martos JM. Fibromyalgia: A Review of the Pathophysiological Mechanisms and Multidisciplinary Treatment Strategies. Biomedicines 2024;12:1543.
2. D'Amuri A, Greco S, Pagani M, Presciuttini B, Ciaffi J, Ursini F. Common non-rheumatic medical conditions mimicking fibromyalgia: A simple framework for differential diagnosis. Diagnostics. 2024;14:1758.
3. Palazzo D, Biliotti E, Esvan R, et al. Vitamin D deficiency and health-related quality of life in chronic hepatitis C. J Viral Hepat. 2019;26:774-7.
4. Palazzi C, D'Amico E, D'Angelo S, Gilio M, Olivieri I. Rheumatic manifestations of chronic hepatitis C virus infection: Indications for a correct diagnosis. World J Gastroenterol. 2016;22:1405-10.
5. Dadabhai AS, Saberi B, Lobner K, Shinohara RT, Mullin GE. Influence of vitamin D supplementation on liver fibrosis in patients with chronic hepatitis C: A systematic review and meta-analysis of the pooled clinical trial data. World J Hepatol. 2017;9:278-87.
6. Jolliffe DA, Stefanidis C, Wang Z, et al. Vitamin D metabolism is dysregulated in asthma and chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2020;202:371-82.
7. Hoan NX, Tong HV, Song LH, Meyer CG, Velavan TP. Vitamin D deficiency and hepatitis virus-associated liver diseases: a literature review. World J Gastroenterol. 2018;24:445-60.
8. Makrani AH, Afshari M, Ghajar M, Forooghi Z, Moosazadeh M. Vitamin D and fibromyalgia: a meta-analysis. Korean J Pain. 2017;30:250-7.
9. Bjelakovic M, Nikolova D, Bjelakovic G, Gluud C. Vitamin D supplementation for chronic liver diseases in adults. Cochrane Database Syst Rev. 2021;8:011564.
10. Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum.1990;33:160-72.
11. Sarmer S, Ergin S, Yavuzer G. Validity and Reliability of the Turkish version of the Fibromyalgia Impact Questionnaire. Rheumatol Int. 2000;20:9-12.
12. Kücükdeveci AA, McKenna SP, Kutlay S, Gürsel Y, Whalley D, Arasil T. The Development and psychometric assessment of the Turkish version of the Nottingham Health Profile. Int J Rehabil Res. 2000;23:31-8.
13. Cacoub P, Saadoun D. Extrahepatic manifestations of chronic HCV infection. N Engl J Med. 2021;384:1038-52.

14. Moretti R, Caruso P, Dal Ben M, Gazzin S, Tiribelli C. Hepatitis C-related cryoglobulinemic neuropathy: potential role of oxcarbazepine for pain control. BMC Gastroenterol. 2018;18:19.

15. Varrassi G, Rekatsina M, Perrot S, et al. Is fibromyalgia a feasible diagnosis or a Medical Mystery? Cureus. 2023;15:44852.

16. Falak S, Aftab L, Saeed M, Islam A. Prevalence of vitamin D deficiency is related to the severity of liver damage in Hepatitis-C patients. Pak J Med Sci. 2020;36:445-50.

17. Méndez-Sánchez N, Coronel-Castillo CE, Ramírez-Mejía MM. Chronic Hepatitis C virus infection, extrahepatic disease, and the Impact of New Direct-Acting Antivirals. Pathogens. 2024;13:339.

18. Mohamed AA, Abd Almonaem ER, Mansour AI, Algebaly HF, Khattab RA, El Abd YS. Importance of Studying the Levels of Hepcidin and Vitamin D in Egyptian Children with Chronic Hepatitis C. J Transl Int Med. 2019;7:15-21.

19. Labenz C, Toenges G, Schattenberg JM, et al. Health-related quality of life in patients with compensated and decompensated liver cirrhosis. Eur J Intern Med. 2019;70:54-9.

20. Elbadry M, Badawi M, Youssef N, et al. Impact of treating chronic hepatitis C with direct acting antivirals on health-related quality of life: a real-life Egyptian experience. Egyptian Liver Journal. 2024;14:14.

21. Honrubia López R, Madejón Seiz A, Romero Portales M, et al. OR 6339 inglés Quality of life study in asymptomatic patients with hepatitis C. Rev Esp Enferm Dig. 2020;112:520-4.

22. Beloborodova EI, Lambrova EG, Beloborodova EV, et al. [Quality of life indices in patients with chronic viral hepatitis]. Ter Arkh. 2010;82:41-5.

23. Heredia-Jimenez J, Orantes-Gonzalez E. Gender differences in patients with fibromyalgia: a gait analysis. Clin Rheumatol. 2019;38:513-22.

24. Kasapoğlu Aksoy M, Altan L, Ökmen Metin B. The relationship between balance and vitamin 25(OH)D in fibromyalgia patients. Mod Rheumatol. 2017;27:868-74.

25. Garip Y, Öztaş D, Güler T. Prevalence of fibromyalgia in Turkish geriatric population and its impact on quality of life. Agri. 2016;28:165-70.