

Research Paper

Sleep Disorder Among Patients With Chronic Liver Disease

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ABSTRACT

Objectives: The aim of the study was to assess the sleep characteristics among patients with chronic liver diseases (CLDs) and find the relationship between variables of their demographic and sleep disorder.

Methods: This descriptive cross-sectional study was designed to achieve the stated goals of patients with CLD in the Al-Najaf Center for Gastroenterology and Hepatology in Al-Sadr Medical City from November 1, 2020, to June 1, 2021. The sample was selected from 120 adult patients ≥ 18 years using non-probability sampling (purposeful) with CLD (disease duration of six months or more). The questionnaire consisted of two socio-demographic parts with clinical data (18 items) and a general health questionnaire (28 items) with 4 implicit subscales, including insomnia and anxiety level.

Results: There was a strong significant relationship between sleep disorder and age ($P=0.001$), occupational status ($P=0.001$), daily activity ($P=0.001$), BMI ($P=0.001$), and duration of disease ($P=0.001$), gender ($P=0.021$), educational level ($P=0.04$), marital status ($P=0.049$), and type of disease ($P=0.01$). However, there was no significant relationship between sleep disorder and the remaining demographic and clinical data.

Discussion: In conclusion, there is a relationship between the sleep disorder of CLD patients and their socio-demographic data. There is a strong significant relationship between patients' physical status and their sleep disorder ($P=0.001$). This result means that the disease has a significant effect on sleep.

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Highlights

- One of the health indicators for this sample is sleep disturbance.
- It is possible to improve the health of these patients and improve the quality of sleep to slow the progression of the disease.
- The increasing number of these patients is not enough to provide medicines and medical supplies, but awareness and support at all levels should be considered.

Plain Language Summary

Not dealing with liver diseases, especially chronic ones, in a realistic and objective manner exacerbates the situation for the worse and makes the patient feel alienated and isolated. Thus, they feel that nobody does engage with them, which is a clear and explicit indication that their condition is getting worse day by day. So recently, the science of medicine and pharmacology is developing in the field of microorganisms and chemistry, and this disease may soon be cured. We just need patience and support for these patients as possible and to find available and inexpensive solutions. Sleep is one of the tools first, in terms of improving mood, and in order to enable the rest of the liver, and second, to maintain and work better during sleep.

1. Introduction

The liver is indispensable for maintaining good all-body functioning, and after the skin, the liver is the largest organ in the human body [1]. The liver can re-grow its own tissue after a cut or injury, and it can work until a large part of it is diseased or damaged [2]. The things that we breathe, drink, eat and enter across the body get filtered through the liver. It also helps to maintain the body's heat to properly function the body. It also plays a key role in the blood clotting process and also stores minerals and vitamins, such as copper and iron and releases them into the blood when needed. It converts the food through eating into energy and gives out chemicals that aid the central nervous system (CNS) and brain, and also accomplishes hundreds of tasks during the day [3].

Chronic liver disease (CLD) is rising annually and increases mortality and morbidity in the world. It is also a complex disease that determines human effectiveness at all ages. In the last decade, the number of people with this disease has increased, about 500 million people are infected with this disease around the world because of viral infections only, and the number is even higher when we add the rest of the causes, such as fatty liver, alcohol, immune diseases, and cryptogenic and metabolic disorders. CLD has a negative effect on health aspects since patients usually have a loss of appetite, indisposition, asthenia, abdominal pain or discomfort, muscle

weakness, joint pain, insomnia, and other complications related to CLD or cirrhosis, e.g. recurrent bleeding in the esophagus and stomach due to varicose veins, ascites, and hepatic encephalopathy (HE). Moreover, CLD is related to impaired job performance, mood swings, impaired functioning, low self-esteem, anxiety, depression, and other psychological or emotional problems that mainly affect mental health and well-being [4].

CLD may lead to the syndrome of HE or portal-systemic shunting (PSS). The HE is a complication of hepatocellular malfunction associated with a changeable degree of shunting through portal-systemic venous. In theory, HE may occur as a result of synthesis by the failing liver of encephalopathogenic materials or their precursors, reduction synthesis by the failure liver of substances essential for normal brain function, and/or reduced extraction or metabolism by the failing liver encephalopathogenic materials or their precursors [5].

Sleep disorder has many dimensions and interactions, particularly it is related to chronic diseases, emotional status, gender, low economic status, educational level, the coexistence of underlying liver diseases, the severity of disease, and period of life expectation, which possibly lead to a decreased mental health functioning, such as sleep disturbances in long-term diseases. CLD has numerous forms, which influence different facets of mental health [6].

The negative impact of CLD on sleep patterns on daily physical functioning has been clear through somnolence daytime and insomnia at night. A practice of intervention connection becomes particularly important with the practice of treatable psychological or physiological status, and recently, several studies have recognized psychological issues related to patients with CLD, such as depression, sleep disturbance, and disease-related worries [7, 8].

In addition to being a long-term chronic condition that can advance to include ascites, esophageal variceal hemorrhage, and hepatic coma, hepatitis liver cirrhosis patients also have a higher chance of developing liver cancer. As a result, the patients may have problems, including chronic pain, psychological stress, and financial hardship. The phenomenon of persistent physical illnesses accompanied by psychological problems, such as anxiety and depression, has drawn considerable attention due to a transformed medical model. However, there is no comprehensive research on the psychological health and sleep patterns of Iraqi people with cirrhosis caused by hepatitis [9].

The severity of disease, loss of future expectations, and poor psychological resources can play in increased psychological distress in people with chronic illnesses, but this still needs to be verified. A numeral of conclusions recommends that individuals with CLD are vulnerable to psychological problems, such as depression, anxiety, obsessive-compulsive disorder (OCD), and daytime sleepiness [10].

Patients with CLD frequently experience sleep disorders [11]. Liver-related silent consequences, such as sarcopenia, hidden HE, and muscular cramps, have been linked to sleep difficulties and frequently lower the QoL of CLD patients. In this study, we assessed the incidence of liver-related sleep issues in CLD patients. The researchers also tried to investigate the relationship between the sleep disorder of CLD patients and their socio-demographic and clinical characteristics.

2. Materials and Methods

Study design

A descriptive cross-sectional study design was carried out to attain the stated objectives from first November 2020 to the first of July 2021.

Study setting

The study was conducted in AL-Najaf province, AL-Najaf AL-Ashraf Health Directorate, AL-Sadder Medical City, at AL-Najaf Gastroenterology and Hepatology Center.

Study sample

A non-probability purposeful sampling of CLD patients (120 cases were excluded due to eight incomplete questionnaires) who attended the center was done and the eligible patients were included.

The study sample was chronic liver patients diagnosed by specialists and non-doubtful patients whose illness lasted for six months or more referring to the mentioned center, conscious and aware, with Arabian nationality. Those who met the following criteria were excluded: Those suffering from other highly advanced diseases, such as cancer, kidney failure, heart failure, and other advanced liver disease, people suffering from a mental illness, and people who were ready for endoscopy or biopsy [12, 13].

Study measurements

An assessment tool was adopted by the investigator to measure the impact of CLD on sleep disorder. The investigator translated the General Health Questionnaire-28 (GHQ-28) [14, 15] from English to Arabic. Translation validity was achieved through forward and backward translation then forwarded to the experts to be reviewed by the translation experts. The investigator obtained both copies in English and Arabic and used them directly after simple modification. The final study instrument consisted of two parts:

Part I with two sections: The first section included a socio-demographic characteristics sheet consisting of ten items, which included age, gender, residence, marital status, number of children, socioeconomic status, educational level, family size, occupation, and the level of daily activity.

The second section contained the clinical characteristics sheet consisting of eight items, including smoking, BMI, alcohol, disease type, duration of disease, reasons for injury, other physical diseases, psychological disease, and sedative abuse.

Part II: The sleep screening instruments: The GHQ-28 is highly used to assess psychological distress, including sleep disorders among patients with chronic and clinical non-psychiatric diseases [16]. The GHQ-28 was produced by Goldberg in 1978 and since then has been converted into 38 languages [17]. It was developed as a screening instrument to distinguish those liable to have or to be at risk of a psychiatric issue. The GHQ-28 is a 28-questions measure of feeling distressed in a medical setting. The questionnaire was modified and developed according to language, culture, and understanding in a simple way. Through element investigation, the GHQ-28 has been partitioned into four sub-scales. It takes under 15-17 minutes to finish [18, 19].

It contains the necessary aspects to examine the psychological state of this group of people, and compared to other questionnaires, it is considered short and easy to assess the patient and the burden of the disease. It consists of four domains, including the first seven items (1-7) assess somatization (e.g. having hot or cold spells), the second seven items (8-14) assess insomnia and anxiety, (e.g. losing much sleep over worry), the third seven items (15-21) assess the social dysfunction (e.g. feeling capable of making decisions about things), and the last seven items (22-28) assess severe depression (e.g. feeling that life is entirely hopeless). This instrument is structured based on previous studies [20, 21].

The data were analyzed with descriptive statistics, and cut-off points for symptomatic (mean 2.5 and more) and asymptomatic (mean less than 2.5) patients, and the significance level was set at $P < 0.05$ and confidence interval (CI) at 95%.

3. Results

Table 1 shows that most of the study subjects were aged 18-35 (43%) and under 50 years. The majority of the study sample was aged 18-53 years (71%). Regarding gender, the number of male cases was more than females (63:49). Majority of study subjects were living in urban regions (82, 73%). Most subjects were married (69%) and 75% of the participants had children.

Concerning the monthly income, 57% reported enough to some limit, while 32% reported not enough. Also, 22% had a primary school education while 19% had a college or institute education. In addition, most of them had 5-9(64%) family members. Regarding occupation status, 55% were an employee. In addition, most study samples had moderate physical activity (47%).

Table 2 shows that the majority of participants were no smokers (96%). Most cases had normal BMI (78%). All study subjects reported no alcohol consumption. Also, concerning type of disease, more than half had hepatitis B virus (HBV) (58%), some of them (8%) had cirrhosis, (9%) had hepatitis C virus (HCV) and cirrhosis, and 2% had carcinoma and cryptogenic. Regarding the duration of the disease, for the majority, it was less than one year (42%). Regarding the reason/s for disease, most of the participants did not know the reason (71%). In addition, the majority of cases were not suffering from other physical diseases (71%). No psychiatric disease and no drug abuse were found.

Table 3 shows responses to the anxiety and insomnia domain, the subject's responses to this domain were mainly symptomatic (Figure 1) for the following items: Do you lose a lot of sleep over worry? Do you have dif-

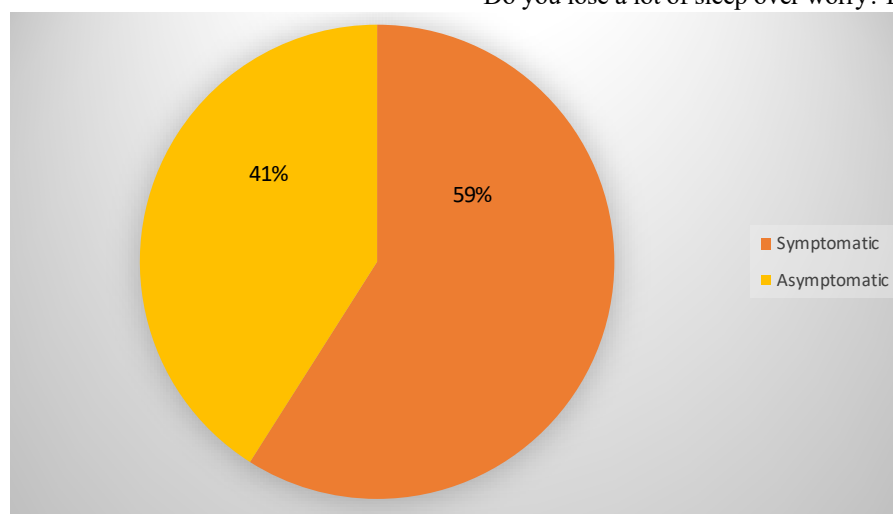


Figure 1. Sleep disorder index. Most of the participants were symptomatic sleep disorders.

Table 1. Demographic data of samples (n=112)

Demographic Data	Rating and Intervals	No. (%)
Age (y)	18-35	43(38)
	36-50	37(33)
	51-64	25(23)
	65 and more	7(6)
Gender	Male	63(56)
	Female	49(44)
Residency	Urban	82(73)
	Rural	30(27)
Marital status	Single	24(21)
	Married	77(69)
	Divorced	5(4)
	Widowed	6(6)
Number of children	No	28(25)
	1-2	17(15)
	3-4	41(37)
	5≤	26(23)
Economic status (monthly income)	Enough	12(11)
	Enough to some extent	64(57)
	Not enough	36(32)
Educational levels	Illiterate	7(6)
	Able to read	6(5)
	Able to read and write	15(13)
	Primary school	25(22)
	Intermediate school	21(19)
	Secondary school	18(16)
	Institute or college	20(19)
Number of Family members	1-2	1(0.9)
	3-4	13(12)
	5-9	72(64)
	10-15	21(19)
	16≤	5(4.1)
Occupation	Employee	62(55)
	Unemployed	50(45)
Levels of Daily Activity	Setting (long-standing)	1(0.9)
	Mild activity	14(12.1)
	Moderate Activity	52(47)
	High activity	45(40)

Table 2. Clinical data of the sample (n=112)

Clinical Data	Rating and Intervals	No. (%)
Smoking	Yes	5(4)
	No	107(96)
Body mass index (BMI)	Underweight	11(10)
	Normal weight	87(78)
	Overweight	14(12)
Alcohol	No	112(100)
Disease type	HBV with cirrhosis	9(8)
	HBV without cirrhosis	49(44)
	HCV with cirrhosis	10(9)
	HCV without cirrhosis	32(30)
	Carcinoma	3(2)
	Autoimmune	6(5)
	Cryptogenic	3(2)
Duration of disease	Less than one year	46(42)
	1>2	40(35)
	2>3	16(14)
	3≥	10(9)
Reason/s of injury	I do not know	79(71)
	Blood transfusion	20(18)
	Wounds or injections	10(9)
	Sexual intercourse	3(2)
Suffering from Physical Diseases	No	78(71)
	Hypertension	10(9)
	DM	10(9)
	Renal failure	4(3)
	Heart failure	5(4)
	Others	5(4)
Psychiatric disease	No	112(100)
Drug abuse	No	112(100)

Table 3. Patients' responses to the anxiety and insomnia domain items

Items	Sum	Mean±SD	RS%	Assessment
Do you lose a lot of sleep over worry?	343	2.52±0.95	60.39	Symptomatic
Do you have difficulty staying asleep once you are off?	367	2.78±0.94	64.61	Symptomatic
Are you constantly under pressure?	282	1.99±0.88	49.65	Asymptomatic
Are you getting edgy and bad-tempered?	403	2.84±0.80	70.95	Symptomatic
Are you getting scared or panicky for no good reason?	378	2.76±0.94	66.55	Symptomatic
Do you find everything getting on top of you?	407	2.87±0.89	71.65	Symptomatic
Do you feel nervous or strung up all the time?	358	2.72±0.94	63.03	Symptomatic

Symptomatic (mean ≥ 2.5) and asymptomatic (mean < 2.5), *RS: Relative sufficiency.

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difficulty staying asleep once you are off? Are you getting edgy and bad-tempered? Are you getting scared or panicky for no good reason? Do you find everything getting on top of you? Do you feel nervous or strung up all the time? , while they were asymptomatic for Do you lose a lot of sleep over worry? and Are you constantly under pressure?

Table 4 shows that the patients' overall responses to anxiety and insomnia domain were symptomatic of psychosocial status.

Table 5 shows that there was a strong significant relationship between physical status and psychosocial aspects (anxiety and insomnia) ($P=0.01$).

Table 6 shows the Pearson's correlation coefficient between patients' physical status and their psychosocial aspects. There was a significant correlation between physical status and anxiety and insomnia ($r=0.661$), and overall, Pearson's correlation coefficient was highly significant in the physical domain ($r=0.731$).

Table 7 reveals that there was a strong significant relationship between the patients' sleep disorder index and their age ($P=0.001$), occupational status ($P=0.001$), daily activity ($P=0.001$), BMI ($P=0.001$), duration of

disease ($P=0.001$), gender ($P=0.021$), educational level ($P=0.04$), marital status ($P=0.049$), and type of disease ($P=0.01$). While there was no significant between the remaining demographic and clinical data.

4. Discussion

Part I: Demographic data related to the CLD patients

Regarding age, the most common group age group was 18-35 years (38%) followed by the age group of 36-50 years (33%). Most samples were under 50 years of age (71%), which is similar to other studies, e.g. Liu et al. and Hajarizadeh et al., who reported that the predominant age of the study samples was 43.87 ± 13.31 and 45 years, respectively, Alsamara et al. reported the mean age of 26.7 ± 4.9 , which can indicate the fact that the CLD patients are mostly young and middle-aged, compared to the rest of chronic diseases that are in the final stages of life; for example, atherosclerosis, blood pressure, and strokes [21–23].

Regarding gender, the result revealed that the number of male cases was more than females (56% vs. 44%), as

Table 4. Assessment of patients' overall responses to the anxiety and insomnia domain items

Variable	Levels	No. (%)	Mean	Assessment
Anxiety and insomnia domain	Symptomatic	66(59)	2.62	Symptomatic
	Asymptomatic	46(41)		
	Total	112(100)		

Symptomatic (mean 2.5 and more) and asymptomatic (mean < 2.5)

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Table 5. Relationship between the patients’ physical status and their sleep disorder

Sleep Index	Rating	Physical Status		Chi-Square Value	df	P
		Symptomatic	Asymptomatic			
Anxiety and insomnia	Symptomatic	73	11	24.930	1	0.001 ^{HS}
	Asymptomatic	28	30			
	Symptomatic	48	38			
	Asymptomatic	29	33			

^{HS} Highly significant at P≤0.01

demonstrated by some studies, such as Popovi et al. and Perkins (56% of patients were male) and (57%). It can be concluded that men are more likely than women to develop chronic diseases (CLD). Also, men are more prone to injuries and diseases, especially with socioeconomic burdens, long periods of heavy work, and indifference to disasters or injuries [24-26].

Chronic hepatitis C virus (CHCV) is a significantly more stressful life event [4] and sleep disturbance and anxiety that are correlated with the patients’ demographic characteristics, such as loss of the source of income, divorce, or unemployment. It is suggested that pre- and post-test psychosocial support and counseling would help to reduce the stress and anxiety associated with CHCV [3].

The results also showed that most of the people involved were from the urban regions (73%) and supported the results of several studies; for example, Goyal et al. This finding indicates that CLD is a modern disease and spreads in urban regions because of the ease of movement of people from one place to another and the density of people exposed to the same area with infected people [27].

The results also revealed that most of the study subjects were married (69%), followed by single (21%) and divorced and widowed (10%). This result is consistent with some other studies e.g. Batista-Neves et al. [28]. Also, Batista-Neves et al. indicated that 37% of the study sample had 3-4 children while 25% had no children [28].

Regarding economic status, most participants reported enough outcomes (57%) while the remaining reported not enough (32%); this result agrees with studies by Gitto et al. and Alsamarai et al. who reported that a rise in the prevalence of disease correlated with low socioeconomic levels. This suggests that most of the infections of this disease are among middle- and low-income families, which may be more susceptible to illnesses because of the demand for living and facing the difficulties of life [24, 29].

Concerning educational level, most participants had primary school education (22%), followed by below primary school (24%). This result agrees with that of Hasan et al., and Hajarizadeh et al., who suggested the increased prevalence of CLD in cases with low educational levels or illiterates [22, 30].

Table 6. Correlation between the patients’ physical status and their psychosocial aspects

Studied Domains	Statistical Parameters	Physical	Anxiety and Insomnia	Overall Psychosocial and Physical Status
Physical	Pearson correlation	1	0.661	0.731
	P (2-tailed)		0.001	0.001
Anxiety and insomnia	Pearson correlation	0.661	1	0.889
	P (2-tailed)	0.001		0.001
	P (2-tailed)	0.001	0.001	

Non-significant at P>0.05; significant at P<0.05; highly significant at P≤0.01

Table 7. Association between the patients' sleep disorder and their demographic and clinical data

Demographic and Clinical Data	Chi-Square Value	d _f	P
Age (y)	15.702	3	0.01 ^{HS}
Gender	5.348	1	0.021 ^S
Residency	0.847	1	0.357 ^{NS}
Marital status	7.839	3	0.049 ^S
Number of children	2.217	3	0.529 ^{NS}
Economic status	6.948	2	0.084 ^{NS}
Educational levels	19.303	6	0.04 ^S
occupational status	11.452	1	0.001 ^{HS}
Daily activity	21.486	3	0.001 ^{HS}
Smoking	3.436	1	0.61 ^{NS}
Body mass index	32.052	2	0.001 ^{HS}
Disease type	13.341	6	0.010 ^S
Duration of disease	17.611	3	0.001 ^{HS}
Reason of disease	6.805	3	0.078 ^{NS}
Other physical diseases	2.136	3	0.545 ^{NS}

^{NS} Non-significant at $P > 0.05$; ^S Significant at $P < 0.05$; ^{HS} Highly significant at $P \leq 0.01$

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Most subjects reported a family size of 5-9 (64%). This result agrees with another study that indicates that unplanned family size is associated with more psychological distress, especially if it is accompanied by chronic diseases [31].

The results indicated that 55% of the participants are workers, and most of them were male 74, and most of them 58% were engaged in construction work, shops, taxi driving, and other non-governmental jobs only 20 individuals were state employees and had a monthly salary. This result pointed out that those with low economic status are more exposed to infectious diseases, which agrees with other reports [32].

Regarding daily activity, 47% had a moderate activity that may affect the sleep-wake cycle due to continuing lying in bed, and this result agrees with that of Talley et al. and Checton et al. who mentioned that approximately one-quarter of individuals with chronic diseases have one cause or more limitations of daily activity. On the other hand, the complications of the disease itself, such as ascites, pain, disability, fatigue, and/or the side effects of treatment, limit the patient's movement or make him unable to move to meet his personal and family needs [33, 34].

Part II: Clinical data related to chronic liver disease patients

Regarding BMI, 78% had normal weight, followed by 12% for overweight. This result corresponds with that of Moscatiello et al. and Stapleton et al. This result reveals a significant relationship between sleep disorder and BMI, especially for over body weight, which means mood and sleep disorders are linked to increased body fluids [35, 36].

Concerning with type of CLD, most of the subjects had chronic viral hepatitis B and C (58% and 42%, respectively), and 19% of them had cirrhosis liver disease. Regarding chronic hepatitis, there is no statistically significant relationship between hepatitis B and C and sleep disorders. While a significant number of cirrhosis patients have sleep disorders [22, 23, 37].

Regarding the duration of disease, the result revealed that the majority of the study subjects (42%) reported less than one year, besides, the value decreases at the time of infection, which indicates that new infections occur continuously. This result agrees with other studies [38, 39] that claimed that about four million cases annually are newly infected.

Concerning the reason for the disease, most cases did not know the reason (71%). Most of them told the researchers that it can be due to visiting a dentist or surgeon many years ago, and some of them reported due to the operation performed 30 years ago and they had no symptoms and the injury was discovered by chance or routine examination for marriage [27].

Regarding suffering from other physical diseases, most of them (71%) had no organic or chronic problems; thus, the reason is that the sample was less than 50 years old and already had no other chronic diseases. This result is in line with the findings of Stapleton [37].

Part III: Patients' overall responses to psychological aspects

There is a relationship between the patient's physical condition and sleep disorder and means that the disease has a significant impact on both psychological and physical well-being aspects through the individual's inability to sleep. The current finding was supported by other studies [22], which claimed that 49% of the study samples had at least one or more psychiatric comorbidities; physical problems with psychological distress. On the other hand, some psychiatric patients use a treatment causing liver injury or even cirrhosis, such as mood stabilizers, neuroleptics, and a few anti-anxious or antidepressant agents [40].

Insomnia and anxiety

The participant's responses to this questionnaire were mainly effective or symptomatic for items 1, 2, 4, 5, 6, and 7, while asymptomatic for item 3. Sleep disturbances, such as early insomnia or sleepiness during the day, are certain signs of CLD due to using long-term treatment regimens or stress of disease that affect circadian rhythm disorders. This result agrees with many studies [28, 41–42].

From the researchers' point of view, to better understand the pathophysiology of each sleep disorder in line with its etiology, prospective studies are required. Therefore, a more personalized approach may be successful in diagnosing and treating sleep disorders experienced by CLD patients. However, the progress of life and the QoL will improve, because it is widely known that sleep disorders cause patients a great deal of psychological deterioration and also exacerbate liver disease.

5. Conclusion

Sleep disorders occur more commonly among patients with CLDs and are associated with poor mental health. This study showed that the more severe the liver disease, the worse the sleep disturbance. Moreover, this is the first study in Najaf Al-Ashraf province that evaluated sleep in a group of patients with different stages of CLDs. In this regard, the researchers indicated that the results can be verified by other studies; for example, sleep disturbance in this group cannot be confirmed as a result of a pathological process or psychological reaction to what this patient faces of discrimination or change in his/her appearance under the pressure of relatives or friends.

Limitations

Because of waiting for test results, entering a doctor, or the stigma of the disease, all patients could not refer to the specialized center for gastroenterology and hepatology.

Ethical Considerations

Compliance with ethical guidelines

The study was approved by the Research Ethics Committee of the College of Nursing/University of Babylon (Code: 2399). The participants were briefed on the study verbally and to protect their privacy and confidentiality, all data were collected anonymously.

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Authors' contributions

Conceptualization and supervision: Firas Al-aboudy and Hasan Baiee; Methodology: Firas Kanawy; Investigation, writing original draft, review & editing: All authors; Data collection: Firas Kanawy, and Rasha Azez; Data analysis: Firas Kanawy and Hasan Baiee.

Conflict of interest

There is no conflict of interest, according to the authors.

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