Available online at www.medicinescience.org

ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2023;12(1):127-32

Non-alcoholic fatty liver disease and sleep quality: a single center cross-sectional survey study

Zeynep Gok Sargin, Guray Ceylan

Zonguldak Bülent Ecevit University, Faculty of Medicine, Department of Gastroenterology and Hepatology, Zonguldak, Türkiye
Zonguldak Bülent Ecevit University, Faculty of Medicine, Department of Internal Medicine, Zonguldak, Türkiye

Received 30 August 2022; Accepted 04 November 2022
Available online 30.01.2023 with doi: 10.5455/medscience.2022.08.203

Abstract

Sleep-wake disorders are probably a part of Nonalcoholic Fatty Liver Disease (NAFLD) etiology. This study aimed to evaluate the relationship between NAFLD and the Pittsburgh Sleep Quality Index (PSQI) components. Sleep quality was assessed by the PSQI, which comprised seven components. Participants diagnosed with hepatic steatosis using ultrasonographic imaging and healthy volunteers were given the questionnaire. The percentage of subjects with poor sleep quality was noticeably higher in the NAFLD patients than in the non-NAFLD control group (OR: 4.58, 95% CI: 2.67-7.85) ($p<0.001$). Compared to the control group, the NAFLD group reported shorter sleep duration ($p=0.044$), a longer sleep onset delay ($p<0.001$), worse subjective sleep quality ($p<0.001$), a higher percentage of subjects with sleep disturbances ($p<0.001$), a higher percentage of subjects using hypnotic drugs ($p=0.009$), and a higher percentage of subjects with daytime dysfunction ($p<0.001$). When the subjects were split into two groups based on gender, global PSQI sleep quality and subjective sleep quality were significantly worse in both genders with NAFLD than in the non-NAFLD group ($p<0.001$). The sleep onset delay of the NAFLD group was substantially longer in males ($p=0.002$) and females ($p<0.001$) compared to controls. Sleep disturbances were significantly higher in both sexes with NAFLD compared to controls ($p<0.001$). The rate of those with daytime dysfunction in the NAFLD group was considerably higher in both genders compared to the non-NAFLD group ($p=0.001$). Only among the male patients in the NAFLD group the prevalence of hypnotic drug use was substantially greater ($p=0.033$) than in the non-NAFLD group. Poor sleep was associated with NAFLD in both genders.

Keywords: Nonalcoholic fatty liver disease, sleep quality, sleep disturbance, sleep onset delay, sleep duration, daytime dysfunction

Introduction

With an estimated 32.4% global prevalence, the most common chronic liver disease is a non-alcoholic fatty liver disease (NAFLD) [1]. NAFLD has extrahepatic consequences like cardiovascular disease, extrahepatic cancers, and hepatic complications like cirrhosis and hepatocellular carcinoma [2]. Despite liver biopsy being the best technique for assessing NAFLD, it is rarely used due to the cost and risk of complications. The diagnosis is mainly based on radiological imaging after excluding other liver diseases [3]. Unhealthy diets and sedentary lifestyles are blamed for the pathogenesis of NAFLD [4].

However, sleep disturbance has received less attention in the etiology of NAFLD than diet or physical exercise. Sleep-wake disruption is believed to contribute to the pathophysiology of NAFLD [5]. Short sleep duration and obstructive sleep apnea (OSA) have been identified as NAFLD-related factors [6,7].

CITATION
Gok Sargin Z, Ceylan G. Non-alcoholic fatty liver disease and sleep quality: a single center cross-sectional survey study. Med Science. 2023;12(1):127-32

Corresponding Author: Zeynep Gok Sargin, Zonguldak Bülent Ecevit University, Faculty of Medicine, Department of Gastroenterology and Hepatology, Zonguldak, Türkiye,
Email: drszeynepgok@yahoo.com

DOI: 10.5455/medscience2022.08.203

Sleep disruption has been shown to increase the body mass index (BMI) by causing a decrease in leptin and an increase in ghrelin, which are hormones that affect the appetite center [8]. OSA is associated with developing NAFLD regardless of obesity or other common risk factors. Oxidative stress from tissue hypoxia induced by sleep disruption can cause inflammation, mitochondrial malfunction, and sympathetic nervous system hyperactivity. Hepatic steatosis, fibrosis, insulin resistance, and atherosclerosis have all been linked to intermittent hypoxia [9]. As a result, lifestyle diseases can be avoided by early detection and treatment of sleep disorders.

Studies on the relationship between NAFLD and sleep quality are limited in other countries [10–13]. Furthermore, no study could be found on this subject in our country. The effect of sleep duration and quality on NAFLD may also differ according to gender [11,13,14]. The Pittsburgh Sleep Quality Index (PSQI) is a well-known and often-used tool for evaluating sleep quality, which is composed of seven different components; sleep quality, sleep onset delay, sleep duration, sleep disturbance, habitual sleep effectiveness, usage of hypnotic drugs, and daytime dysfunction [15]. The links between each PSQI component and NAFLD are not fully realized. This study aimed to evaluate the relationship between NAFLD and PSQI components.

Material and Methods

Patients

This study was carried out in the gastroenterology and internal medicine clinics of Zonguldak Bulent Ecevit University Hospital between 1 May and 15 August 2022. Patients without chronic liver disease and with fatty liver on ultrasonographic imaging were included in the study as the NAFLD group. Those under 18 years of age, those with viral hepatitis, autoimmune or metabolic liver disease, alcohol consumption (any amount), and a history of malignancy were excluded from the study. Volunteers without hepatic steatosis in the ultrasonographic imaging who applied for check-ups were included in the control group (non-NAFLD group).

A face-to-face PSQI questionnaire of 18 questions was administered to the participants. In addition, liver ultrasonography results, demographic characteristics (gender, age, comorbidities, BMI, smoking habits, daily exercise habits, AST (Aspartate Aminotransferase), ALT (Alanine transaminase), GGT (Gamma-glutamyl transferase) and PLT (platelet counts) results were recorded. According to these parameters FIB-4 index was calculated.

Measurements

According to a widely accepted guideline [16], ultrasonography was used to determine NAFLD. In addition, the degree of hepatic steatosis was recorded as mild, moderate, and severe ultrasonographically [17]. The formula used to determine the FIB-4 score was as follows: FIB-4 score = [(age x AST) / (PLT x √ALT)]. Regular physical exercise was defined as the exercise performed for at least 40 minutes at least three days a week.

Subjective sleep quality, sleep onset delay, sleep duration, sleep disturbance, habitual sleep effectiveness, usage of hypnotic drugs, and daytime dysfunction were the seven components of the PSQI Scale, which consisted of 18 self-administered items. In scoring the PSQI, seven component scores are derived, each scored 0 (no difficulty) to 3 (severe difficulty). The component scores are summed to produce a global score. A global score of greater than five was used to identify people who had poor sleep quality. Subjective sleep quality, component 1 (0 indicates extremely good, 1 indicates quite good, 2 indicates quite bad, and 3 indicates extremely bad). Sleep onset delay, component 2 was described as the total of the scores of the duration needed each night to get to sleep (0 for the first 15 minutes, 1 for the next 16 to 30 minutes, 2 for the next 31 to 60 minutes, and 3 for longer than 60 minutes.) and the likelihood of failing to fall asleep in 30-minute period (0 represents not in the previous month, 1 represents a maximum of once weekly, 2 represents a maximum of twice weekly, and 3 represents a minimum of three weekly occurrences). Sleep duration, component 3; (0 for longer than seven hours, 1 for six to seven hours, 2 for five to six hours, and 3 for less than five hours). Habitual sleep effectiveness, component 4 was described as the ratio of sleeping to lying in bed (0 represents more than 85%, 1 represents 75%–84%, 2 represents 64%–74%, and 3 represents less than 65%). Sleep disturbance, component 5, was described as having difficulty sleeping for different reasons (0 represents not in the previous month, 1 represents a maximum of once weekly, 2 represents a maximum of twice weekly, and 3 represents a minimum of three weekly occurrences). Usage of hypnotic drugs, component 6; (0 represents not in the previous month, 1 represents a maximum of once weekly, 2 represents a maximum of twice weekly, and 3 represents a minimum of three weekly occurrences). Daytime dysfunction, component 7 was described as the total of the scores of unable to maintain staying awake when driving, eating, or participating in social activities (0 represents not in the previous month, 1 represents a maximum of once weekly, 2 represents a maximum of twice weekly, and 3 represents a minimum of three weekly occurrences) and having difficulty maintaining sufficient eagerness to complete tasks (0 represents no problem, 1 represents only minor problem, 2 represents a moderate problem, 3 represents serious problem).

Statistical analysis

The statistical analysis was performed using SPSS (Statistical Package for Social Sciences), version 22. Data were presented as numbers (%), means ±standard deviations. Comparing categorical data was performed using the Chi-square test. The Shapiro-Wilk and Kolmogorov-Smirnov tests were employed to determine whether continuous variables had a normal distribution. Mann-Whitney U test was utilized to compare continuous variables with non-normal distribution. Logistic regression analysis was used to assess the association between NAFLD and sleep quality and control for any confounding variables. A p-value of less than 0.05 was used to demonstrate statistical significance.

DOI: 10.5455/medscience2022.08.203

Ethics

The present study was approved by the non-invasive clinical research ethics committee of the Zonguldak Bulent Ecevit University Faculty of Medicine (Protocol No: 2022/08, Approval date: 20/04/2022). The study protocol adheres to the 1964 Declaration of Helsinki's ethical criteria.

Results

Demographic characteristics of participants

This study included 228 patients with NAFLD and 136 participants without NAFLD as a control group. Patients with NAFLD were older and more obese than the control group, respectively (p<0.001) (p<0.001). ALT, AST, GGT levels, and FIB4 scores were higher in the NAFLD group than in the control group, respectively (p<0.001), (p<0.001), (p<0.001), (p<0.001). The proportion of patients who exercised regularly and had diabetes mellitus (DM) and hypertension (HT) was higher in the NAFLD group, respectively (p=0.036) (p<0.001) (p<0.001) (Table 1).

Sleep quality of participants

The PSQI global score of NAFLD patients was noticeably higher than the control group (p<0.001). Multivariate logistic regression analysis revealed that patients in the NAFLD group had considerably higher odds of having a PSQI score of 5 or above (poor sleep quality) than the patients in the control group (OR: 4.58, 95% CI: 2.67-7.85), (p<0.001) (Table 2).

Compared to the control group, the NAFLD group reported shorter sleep duration (p=0.044), a longer sleep onset delay (p<0.001), worse subjective sleep quality (p<0.001), a higher percentage of subjects with sleep disturbances (composed of components such as waking up early at night, going to the toilet, having difficulty breathing, snoring, having bad dreams, and feeling extremely hot or cold) (p<0.001), a higher percentage of subjects using hypnotic drugs (p=0.009), and a higher percentage of subjects with daytime dysfunction (p<0.001) (Table 3).

Table 1. Demographic characteristics of participants

		NAFLD Group (n=228)	Non-NAFLD Group (n=136)	p-value
Gender	**Male, n (%)**	108 (47.4%)	64 (47.1%)	
	Female, n (%)	120 (52.6%)	72 (52.9%)	0.954
Age, years ± SD		48±13.4	37.3±14.9	<0.001
BMI (kg/m²) ± SD		30±5.7	24.8±4.45	<0.001
Exercise, n (%)		54 (23.7%)	46 (33.8%)	0.036
Smoking n (%)		64 (28.1%)	46 (33.8%)	0.248
DM, n (%)		76 (33.3%)	8 (5.9%)	<0.001
HT, n (%)		62 (27.2%)	6 (4.4%)	<0.001
ALT (IU/l) ± SD		31.18±27.6	16.59±8.23	<0.001
AST (IU/l) ± SD		24.65±11.43	17.99±5.65	<0.001
GGT (IU/l) ± SD		46.31±56.18	16.85±9.1	<0.001
FIB-4 ± SD		1.01±0.77	0.74±0.56	<0.001

NAFLD: Non-Alcoholic Fatty Liver Disease, BMI: Body-Mass Index, DM: Diabetes Mellitus, HT: Hypertension, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, GGT: Gamma Glutamyl Transferase, FIB-4: Fibrosis 4-Score

Table 2. Multivariate logistic regression analysis of risk factors for NAFLD

	p-value	OR	95% CI	
Age	0.059	1.020	0.999	1.041
Gender	0.718	1.105	0.642	1.902
BMI	<0.001	1.150	1.091	1.213
Exercise	0.215	0.695	0.391	1.236
DM	0.005	3.598	1.478	8.759
HT	0.016	3.973	1.290	12.240
Sleep Quality	<0.001	4.586	2.676	7.859

BMI: Body-Mass Index, DM: Diabetes Mellitus, HT: Hypertension, NAFLD: Non-Alcoholic Fatty Liver Disease, OR: Odds Ratio, CI: Confidence Interval

DOI: 10.5455/medscience2022.08.203

Table 3. Sleep quality of participants according to the PSQI components

	NAFLD Group	Non-NAFLD Group	p-value
Subjective sleep quality	1.46±0.76	0.79±0.56	<0.001
Sleep latency	1.24±0.98	0.6±0.79	<0.001
Sleep duration	0.78±1.05	0.47±0.68	0.044
Habitual sleep efficiency	0.38±0.88	0.19±0.58	0.071
Sleep disturbance	1.55±0.68	1.0±0.46	<0.001
Using hypnotic drugs	0.24±0.74	0.07±0.43	0.009
Daytime dysfunction	1.18±1.12	0.56±0.78	<0.001
Global PSQI score	6.89±3.64	3.72±2.49	<0.001
Sleep Quality			
Well	64 (28%)	90 (76.2%)	<0.001
Poor	164 (72%)	46 (33.8%)	

NAFLD: Non-Alcoholic Fatty Liver Disease PSQI: Pittsburgh Sleep Quality Index

When the subjects were split into two groups based on gender, global PSQI sleep quality was significantly worse in patients with NAFLD for males (p<0.001) and females (p<0.001). Subjective sleep quality in both men (p<0.001) and women (p<0.001) was worse in the NAFLD group compared to controls. The sleep onset delay of the NAFLD group was substantially longer in males (p=0.002) and females (p<0.001) compared to controls. Sleep disturbances were considerably higher in both men (p<0.001) and women (p<0.001) with NAFLD compared to controls. Only among the male patients in the NAFLD group, the prevalence of hypnotic drug use was substantially greater (p=0.033) than in controls. The proportion of subjects with daytime dysfunction in men (p=0.001) and women (p=0.001) in the NAFLD group was substantially higher than in the controls (Table 4).

Table 4. Sleep quality of participants according to the gender

MALE	**NAFLD Group (n=108)**	**Non-NAFLD Group (n=64)**	**p-value**
Subjective sleep quality	1.57±0.74	0.91±0.53	<0.001
Sleep latency	1.22±0.92	0.78±0.83	0.002
Sleep duration	0.89±1.11	0.53±0.8	0.07
Habitual sleep efficiency	0.5±1	0.22±0.55	0.125
Sleep disturbance	1.54±0.63	0.97±0.47	<0.001
Using hypnotic drugs	0.26±0.75	0.06±0.35	0.033
Daytime dysfunction	1.13±1.08	0.53±0.67	<0.001
Global PSQI score	7.19±3.57	4±2.17	<0.001
FEMALE	**NAFLD Group (n=120)**	**Non-NAFLD Group (n=72)**	**p-value**
Subjective sleep quality	1.37±0.78	0.69±0.57	<0.001
Sleep latency	1.25±1.03	0.44±0.73	<0.001
Sleep duration	0.68±1	0.42±0.55	0.325
Habitual sleep efficiency	0.27±0.75	0.17±0.61	0.295
Sleep disturbance	1.57±0.72	1.03±0.44	<0.001
Using hypnotic drugs	0.22±0.74	0.08±0.5	0.131
Daytime dysfunction	1.16±1.23	0.58±0.87	<0.001
Global PSQI score	6.62±3.7	3.47±2.51	<0.001

NAFLD: Non-Alcoholic Fatty Liver Disease PSQI: Pittsburgh Sleep Quality Index

There was no significant difference in sleep quality between patients with mild, moderate, and severe hepatosteatosis (p=0.279).

Discussion

The mechanism for the relationship between sleep quality and NAFLD is unclear. The present study showed that NAFLD patients had worse global sleep quality than the non-NAFLD group. Also, patients with NAFLD were four and a half times more likely to have poor sleep quality than those without. However, the rate of patients with DM, HT, and obesity, which are components of metabolic syndrome, was higher in the NAFLD group. The increase in appetite seen in people with poor sleep quality [8] may increase body mass and consequently

DOI: 10.5455/medscience2022.08.203

comorbidities such as DM and HT. PSQI subcomponents such as subjective sleep quality, sleep duration, sleep onset delay, sleep disturbance, usage of hypnotic drugs, and daytime dysfunction were also observed to be worse in the NAFLD group. These findings were in line with Kim et al.'s [13] and Chou et al.'s [10] results. However, not all components of the PSQI were evaluated in their studies. In the present study, although habitual sleep efficiency was worse in the NAFLD group, statistical significance could not be reached because the NAFLD group spent less time in bed and slept for a shorter time. A Japanese study [11] demonstrated that daytime dysfunction and the usage of hypnotic drugs were related to NAFLD. According to the PSQI subcomponents of that study, only the use of hypnotic medications was linked to NAFLD in both genders. When the NAFLD group in our cohort was subdivided by gender, statistical significance for hypnotic drug use in females could not be reached since the usage of hypnotic drugs in females was likely also higher in the control subjects. This could explain the high rate of hypnotic medication use in this population, as NAFLD patients may use more pharmacotherapy to treat their sleeping problems. Still, it has been emphasized that there is not enough evidence to show that pharmacotherapy improves sleep quality or duration in patients with poor sleep quality [18]. The short sleep duration at night can cause daytime sleepiness and dysfunction throughout the day. In the present study, patients with NAFLD had a greater rate of shorter sleep duration and daytime dysfunction. In a comparison study by Bernsmeier et al. [12] with healthy controls, it was emphasized that daytime sleepiness in NAFLD was correlated with disease severity. Since the body's energy consumption is higher when awake than when sleeping, the increased risk of NAFLD in those with poor-quality sleep and short sleep duration may be related to not consuming enough energy due to problems such as napping the next day.

However, the level of sonographic hepatic steatosis and sleep quality were not associated with the present study. In accordance with the findings of this study, poor sleep quality was associated with both moderate and severe NAFLD in the study by Chou et al. [10] conducted on the Taiwanese population.

Sleep has modulatory effects on hypothalamic-pituitary-adrenal (HPA) axis activity. While the onset of sleep had an inhibitory effect on cortisol secretion, bursts of cortisol secretion were detected during awakening. Sleep deprivation and poor sleep quality cause activation of the HPA axis. HPA hyperactivity is associated with metabolic disorders, and the relationship between sleeping problems and the incidence of obesity and diabetes has been demonstrated [19]. Furthermore, it has been proven that low-quality sleep and high plasma orexin-A concentrations interact to cause changes in body mass index [20]. Adipokines are proteins produced by adipose tissue and have roles in sleep physiology and sleep disorders; conversely, sleep disturbance may affect adipokine functions, possibly contributing to metabolic disorders [21]. Changes in sleep duration or quality are associated with changes in ghrelin or leptin, which affect appetite regulation [22]. The NAFLD group had a higher mean BMI and a greater prevalence of diabetic patients than the control group in our dataset. In patients with DM, poor glycemic control has been demonstrated to be independently related to poor sleep quality [23]. Also, in this study, the rate of HT patients was higher in NAFLD patients than in the non-NAFLD group. It has been established that HT and insomnia are related [24]. In our results, besides sleep disturbance, as in previous studies [25,26], high BMI, DM, and HT were shown as independent risk factors for NAFLD.

In the present study, ALT, AST, GGT levels, and FIB4 scores were also higher in the NAFLD group besides DM and HT. This finding suggests that the patient group included steatohepatitis and fibrosis beyond simple liver steatosis. Additionally, this study found that patients with NAFLD exercised more frequently than those in the non-NAFLD control subjects. This result may be related to the fact that exercise has been recommended as a treatment regimen for this patient population. Although obesity and insulin resistance have been proven to be primary causes of NAFLD [25,26], the results of this study showed that NAFLD and global sleep quality were related after confounding factors such as BMI and DM were removed.

According to our knowledge, this is the first study investigating NAFLD-sleep quality and its subcomponents in our country. However, this study has some limitations. The single-center design and relatively limited sample size were its main limitations. In addition, the fact that it is a survey study with subjective answers requires that objective methods verify the relationships between NAFLD and sleep quality. The brands and dosages of hypnotic drugs used by the patients were not evaluated. Finally, the non-NAFLD group was younger, which may have affected these results.

Conclusion

Poor sleep was associated with NAFLD in both genders. Compared to the non-NAFLD group, the NAFLD group reported shorter sleep duration, a longer sleep onset delay, worse subjective sleep quality, a higher percentage of subjects with sleep disturbances, a higher percentage of subjects using hypnotic drugs, and a higher percentage of subjects with daytime dysfunction.

Conflict of interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical approval
The present study was approved by the non-invasive clinical research ethics committee of the Zonguldak Bulent Ecevit University Faculty of Medicine (Protocol No: 2022/08, Approval date: 20/04/2022). The study protocol adheres to the 1964 Declaration of Helsinki's ethical criteria.

References

1. Riazi K, Azhari H, Charette JH, et al. The prevalence and incidence of

DOI: 10.5455/medscience2022.08.203

NAFLD worldwide: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol. 2022;7:851-61.

2. Hagström H, Kechagias S, Ekstedt M. Risk for hepatic and extra-hepatic outcomes in nonalcoholic fatty liver disease. J Intern Med. 2022;292:177-89.
3. Ando Y, Jou JH. Nonalcoholic Fatty Liver Disease and Recent Guideline Updates. Clin liver Dis. 2021;17:23-8.
4. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018;67:328-57.
5. Marjot T, Ray DW, Williams FR, et al. Sleep and liver disease: a bidirectional relationship. lancet Gastroenterol Hepatol. 2021;6:850-63.
6. Umbro I, Fabiani V, Fabiani M, et al. Association between non-alcoholic fatty liver disease and obstructive sleep apnea. World J Gastroenterol. 2020;26:2669-81.
7. Okamura T, Hashimoto Y, Hamaguchi M, et al. Short sleep duration is a risk of incident nonalcoholic fatty liver disease: a population-based longitudinal study. J Gastrointestin Liver Dis. 2019;28:73-81.
8. Taheri S, Lin L, Austin D, Young T, et al. Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index. PLoS Med. 2004;1:210-7.
9. Mesarwi OA, Loomba R, Malhotra A. Obstructive Sleep Apnea, Hypoxia, and Nonalcoholic Fatty Liver Disease. Am J Respir Crit Care Med. 2019;199:830-41.
10. Chou YT, Cheng HJ, Wu JS, et al. The association of sleep duration and sleep quality with non-alcoholic fatty liver disease in a Taiwanese population. Obes Res Clin Pract. 2018;12:500-5.
11. Takahashi A, Anzai Y, Kuroda M, et al. Effects of sleep quality on non-alcoholic fatty liver disease: a cross-sectional survey. BMJ Open. 2020;10:e039947.
12. Bernsmeier C, Weisskopf DM, Pflueger MO, et al. Sleep Disruption and Daytime Sleepiness Correlating with Disease Severity and Insulin Resistance in Non-Alcoholic Fatty Liver Disease: A Comparison with Healthy Controls. PLoS One. 2015;10:e0143293.
13. Kim CW, Yun KE, Jung HS, et al. Sleep duration and quality in relation to non-alcoholic fatty liver disease in middle-aged workers and their spouses. J Hepatol. 2013;59:351-7.
14. Imaizumi H, Takahashi A, Tanji N, et al. The Association between Sleep Duration and Non-Alcoholic Fatty Liver Disease among Japanese Men and Women. Obes Facts. 2015;8:234-42.
15. Buysse DJ, Reynolds CF, Monk TH, et al. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28:193-213.
16. Wong VWS, Chan WK, Chitturi S, et al. Asia-Pacific Working Party on Non-alcoholic Fatty Liver Disease guidelines 2017-Part 1: Definition, risk factors, and assessment. J Gastroenterol Hepatol. 2018;33:70-85.
17. Ferraioli G, Soares Monteiro LB. Ultrasound-based techniques for the diagnosis of liver steatosis. World J Gastroenterol. 2019;25:6053-62.
18. Kanji S, Mera A, Hutton B, et al. Pharmacological interventions to improve sleep in hospitalised adults: a systematic review. BMJ Open. 2016;6:e012108.
19. 19. Balbo M, Leproult R, Van Cauter E. Impact of sleep and its disturbances on hypothalamo-pituitary-adrenal axis activity. Int J Endocrinol. 2010;2010:759234.
20. Sauchelli S, Jiménez-Murcia S, Fernández-García JC, et al. Interaction Between Orexin-A and Sleep Quality in Females in Extreme Weight Conditions. Eur Eat Disord Rev. 2016;24:510-7.
21. Wei Z, Chen Y, Upender RP. Sleep Disturbance and Metabolic Dysfunction: The Roles of Adipokines. Int J Mol Sci. 2022;23:1706.
22. Littman AJ, Vitiello M V., Foster-Schubert K, et al. Sleep, ghrelin, leptin and changes in body weight during a 1-year moderate-intensity physical activity intervention. Int J Obes (Lond). 2007;31:466-75.
23. Yoda K, Inaba M, Hamamoto K, et al. Association between poor glycemic control, impaired sleep quality, and increased arterial thickening in type 2 diabetic patients. PLoS One. 2015;10:e0122521.
24. Hu Y, Yan Z, Fu Z, Pan C. Associations of Insomnia With Hypertension and Coronary Artery Disease Among Patients With Type 2 Diabetes Mellitus. Front Cardiovasc Med. 2021;8:730654.
25. Younossi Z, Tacke F, Arrese M, et al. Global Perspectives on Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis. Hepatology. 2019;69:2672-82.
26. Rinella ME. Nonalcoholic fatty liver disease: a systematic review. JAMA. 2015;313:2263-73.