Research Article

HEPATOLOGY FORUM

Chronotype, sleep quality, and night-eating in SLD

doi: 10.14744/hf.2023.2023.0034

Chronotype preference, sleep quality, and night-eating behaviors in patients with metabolic dysfunction-associated steatotic liver disease: Assessing the relationship with disease severity and fibrosis

Ayse Sakalli Kani[1], Ahmet Ozercan[1], Haluk Tarik Kani[2], Fatih Eren[3], Kemal Sayar[1], Yusuf Yilmaz[2,4]

[1]Department of Psychiatry, Marmara University School of Medicine, Istanbul, Turkiye; [2]Department of Gastroenterology, Marmara University School of Medicine, Istanbul, Turkiye; [3]Department of Medical Biology, Marmara University School of Medicine, Istanbul, Turkiye; [4]Department of Gastroenterology, Recep Tayyip Erdogan University School of Medicine, Rize, Turkiye

Abstract

Background and Aim: Our primary objective is to examine the variance in chronotype, night-eating patterns, and sleep quality in patients with biopsy-proven metabolic dysfunction-associated steatotic liver disease. In addition, we aim to establish a correlation between these variables and the severity of the disease and fibrosis.

Materials and Methods: Patients who were following up with biopsy-proven metabolic dysfunction associated steatotic liver disease (MASLD) were included in the study. Histologically severe disease is characterized by a Steatosis, Activity, and Fibrosis activity score of ≥3 or the presence of advanced fibrosis (≥F3). Participants who met the inclusion criteria were given the Morningness and Evening Questionnaire (MEQ), the Pittsburgh Sleep Quality Index, and the Night Eating Questionnaire to complete.

Results: A total of 93 patients were included in this study. According to the MEQ, 48 patients were morning type (51.6%), and 42 (45.2%) were neither type. Sleep quality was determined to be inferior in the non-morningness group (p=0.002). A significantly higher proportion of patients with nocturnal eating syndrome had a non-morningness chronotype preference (n=22, 23.7%), compared to those with a morningness chronotype (n=9, 9.7%) (p=0.001). In the multivariate analysis, both age and poor sleep quality had significant impacts on advanced fibrosis, with odds ratios of 1.11 and 3.81, respectively.

Conclusion: Despite the non-morningness chronotype demonstrating poorer sleep quality and a higher prevalence of night-eating behavior, our findings revealed no statistically significant differences in terms of sleep quality, nocturnal eating habits, or chronotype preferences among patients with varying degrees of MASLD severity. On the other hand, advanced fibrosis was significantly impacted by poor sleep quality.

Keywords: Chronotype; night eating behavior; sleep quality; steatotic liver disease.

How to cite this article: Sakalli Kani A, Ozercan A, Kani HT, Eren F, Sayar K, Yilmaz Y. Chronotype preference, sleep quality, and night-eating behaviors in patients with metabolic dysfunction-associated steatotic liver disease: Assessing the relationship with disease severity and fibrosis. Hepatology Forum 2023; 4(3):123–128.

Received: June 30, 2023; **Revised:** July 24, 2023; **Accepted:** August 02, 2023; **Available online:** September 20, 2023

Corresponding author: Yusuf Yilmaz; Recep Tayyip Erdogan Universitesi Rektorlugu, Rize, Turkiye
Phone: +90 533 440 39 95; **e-mail:** dryusufyilmaz@gmail.com

Hepatology Forum - Available online at www.hepatologyforum.org

Introduction

Metabolic dysfunction associated steatotic liver disease (MASLD) is one of the major causes of chronic liver disease worldwide. To date, non-alcoholic fatty liver disease (NAFLD) was routinely used to define the disease. In recent decades, the term NAFLD became insufficient to describe the disease and failed to encompass all aspects of the disorder. MASLD centers on the cardiometabolic risk factors for diagnosis and the presence of steatosis without any other driving factor for liver steatosis.[1] As a result of increasing obesity globally, MASLD is also predicted to become the leading cause of end-stage liver disease and to pose an increasing burden on health systems in the future.

Although the pathogenesis of MASLD has not been fully explained, abnormalities in hepatic energy metabolism, lipid accumulation, inflammation, and oxidative stress have been considered the main pathways.[2] Besides these factors, recent preclinical studies have revealed that the relevant metabolic mechanisms are under circadian control, strongly emphasizing the critical role of circadian abnormalities in the pathogenesis of MASLD and metabolic dysfunction associated steatohepatitis (MASH).[3] Furthermore, it has been stated that candidate drugs being developed for the treatment of MASH modulate chrono disruption by targeting circadian pathways, and chronopharmacology may be a promising tool in the prevention and treatment in the future.[4]

Chronotype is a term used to describe how each individual's circadian rhythm differs in behavioral and biological processes from one another. Humans are divided into three chronotype categories: morning, intermediate, and evening. For individuals with the morningness chronotype, time-oriented fluctuations in daily physiological variables occur earlier in the day than in the intermediate and evening chronotypes (phase advance). In contrast, the shift in these values happens later in the day in those with an eveningness chronotype (phase delay).[5] Social rhythm givers (external zeitgebers), such as bedtimes and mealtimes, are essential in regulating circadian rhythm. Changes in these behavioral patterns may create a mismatch between the environment's endogenous rhythm and time cues, leading to chrono disruption.[6]

Several clinical studies have investigated the relationship between sleep duration and quality and MASLD and revealed that poor sleep quality leads to changes in lipid metabolism.[7] On the other hand, chronotype differences, a crucial behavioral expression of intrinsic circadian preference and express the preferred time for individuals to sleep or per-

form daily activities, are not well-studied in the MASLD population. It has been shown that there is a strong relationship between night eating attitude and obesity; however, only one study examined the relationship between disease severity, fibrosis, and night eating behavior in a limited number of participants.[8]

Considering the aforementioned findings, this study aimed to determine the interrelation between different chronotype preferences with MASLD severity, focusing on the mediating effect of sleep quality and night eating behavior in this relationship. Our second aim was to see whether feeding hours incompatible with the person's chronotype preference would increase MASLD severity.

Materials and Methods

Sample and Study Procedure

We conducted a cross-sectional study on patients aged 18–65 who were followed up at the Marmara University Gastroenterology Outpatient Clinic. Patients who revealed hepatic steatosis by any imaging modality, had elevated aminotransferase levels for at least 6 months, or had existing hepatomegaly or splenomegaly without high liver function tests were subjected to a liver biopsy. Patients whose steatosis was confirmed in liver histology were included in the study. The diagnosis of steatotic liver disease in patients was established through liver biopsy. Patients with any other causes of steatosis were excluded from the study. Those with at least one cardiometabolic risk factor were included in the study.[1] Patients were histologically categorized using the steatosis, activity, and fibrosis (SAF) classification. Patients scoring at least one point for steatosis, lobular inflammation, or ballooning were considered to have MASH. Patients who did not meet the diagnostic criteria for MASH were excluded from the study. A histologically severe disease is characterized by a SAF activity score of ≥3 and/or the presence of bridging fibrosis (F3) or cirrhosis (F4).[9]

We did not recruit patients with mental retardation, another chronic liver disease, psychiatric treatment during the evaluation, or a history of a neurological disorder that may cause sleep disturbance. Since the scales we used in the study were self-reported, necessary information was given to the participants about the scales and they were asked to fill in the scales. However, help was provided by the researcher when it was thought that the participants had difficulty in reading due to any visual impairment or when the existing expressions were not understood by the participants. All patients gave written informed consent, and the local ethical committee approved the study (approval number: 09.2019.370).

Biological Measures

After a detailed anamnesis, we performed a physical examination on all patients. Aspartate aminotransferase, alanine aminotransferase, platelets, albumin, total cholesterol, high-density lipoprotein cholesterol, triglycerides, plasma glucose concentration, and insulin levels were measured following a 12-h fasting period. In addition, anthropometric measures were recorded, including body weight, body mass index (BMI), and waist circumference (WC).

Psychometric Measures

Assessment of Chronotype Preference and Current Sleep Patterns

Chronotype was evaluated using the Morningness and Eveningness Questionnaire (MEQ). The MEQ is a 19-item self-reported questionnaire that measures habitual waking and bedtimes, preferred times of physical and mental performance, and subjective alertness after rising and before going to bed. It is the most frequently used tool to determine morningness-eveningness in human circadian rhythms, both in healthy individuals and in patients. Scores from the MEQ range from 16 to 86. Higher scores indicate more morningness, whereas lower scores show greater eveningness. The MEQ classifies participants scoring between 59 and 86 as morning types, 42–58 as neither, and 16–41 as evening types. The psychometric properties of the Turkish version of the MEQ were tested by Agargun et al.[10] (2007); its validity and reliability were as high as the original version. In addition to chronotype preference, we asked our participants about the average bedtime and wake-up time in the morning. We aimed to evaluate whether the participants' circadian preferences were compatible with their socially required bedtime.

Assessment of Sleep Quality

We assessed sleep quality with the Pittsburgh Sleep Quality Index (PSQI). The PSQI is a 19-item self-rating questionnaire that measures the average monthly subjective sleep quality. Seven clinically determined component scores, each weighted equally from 0 to 3, are created from the 19 questions. Higher scores indicate poorer sleep quality; the seven component scores are summed to obtain a global score ranging from 0 to 21.[11]

Assessment of Night Eating Syndrome

We used the Night Eating Questionnaire (NEQ). The scale assesses morning hunger and timing of first food consumption, food cravings, and control overeating behavior both before bedtime and during nighttime awakenings, percentage of food consumed after dinner, initial insomnia frequency of nocturnal awakenings, ingestion of food, mood disturbance, and awareness of nocturnal eating episodes. All participants answer the first nine questions in the questionnaire. Participants who do not wake up at night or do not have a snack are instructed not to continue to the following questions. Questions 10–12 are answered by the participants who experience night awakenings, and Questions 13 and 14 are answered by the participants who have night-time snacks. Items other than the seventh item in the questionnaire are scored between 0 and 4 using a 5-point Likert-type measurement. In the seventh item, intraday mood changes are questioned, and those who do not experience changes during the day receive 0 points. Items 1, 4, and 14 are reverse-scored. Item 13, which asks about awareness of midnight snacks, is used to distinguish night eating syndrome from a sleep-related eating disorder, but it is not included in the scoring. The total score can range from 0 to 52. Higher values indicate more frequent night eating. The 15th and 16th questions in the questionnaire are recommended as additional questions but are not included in the scoring. The questionnaire has Turkish validity and reliability. The cutoff value is considered to be 18 according to the Turkish version of the NEQ, and participants with a score of 18 and above are identified as having night-eating syndrome (NES).[12]

Data Analysis

All statistical analyses were conducted using SPSS Version 20. The measurement units are expressed as mean±standard deviation (SD) for continuous data if the distribution is normal and as median (range) if the distribution is not normal. Categorical data were expressed in percentages. Pearson and Spearman correlation analyses were used to test the correlation between the continuous variables. The significance of differences was tested using either Student's t-test and Mann–Whitney

U test for continuous variables or Chi-square test for categorical variables. Logistic regression analysis was performed to evaluate the impact of variables on moderate-to-severe steatosis, severe activity, significant fibrosis, advanced fibrosis, and severe disease. For all analyses, a p-value below 0.05 was considered statistically significant.

Results

A total of 93 patients with MASH were enrolled in the study. The sociodemographic characteristics of the population were as follows: The mean age was 46.49±9.77 years, and 30 (32.3%) patients were female. The median education time was 8 (range: 0–18) years. Fifty-five (59.1%) patients graduated from primary school, 17 (18.3%) were from high school, 18 (19.4%) were from university, 2 (2.2%) were postgraduates, and 1 (1.1%) had no education but was literate. Fifty-five (59.1%) patients were working full-time, 2 (2.2%) were part-time, 24 (25.8%) were housewives, or students, 10 (10.8%) were retired, and 2 (2.2%) were not working. Eight (8.6%) patients were working shifts.

We demonstrate the details of the clinical characteristics of patients in Table 1. The mean BMI was 32.34±4.44, and 30 (32.3%) patients were obese. The mean WC was 90.18±14.16 cm. Increased WC was seen in 21 (22.6%) patients. Fifty-one patients (54.8%) had Type 2 diabetes mellitus (DM), 36 (38.7%) had hypertension (HT), and 60 (64.5%) had hyperlipidemia (HL).

Regarding psychometric measurements, the median PSQI score was 5 (1–16). The mean NEQ score was 14.79±6.27. The median chronotype score of the population was 59 (range: 39–69). When we asked about usual bedtimes, 5 patients (5.4%) reported going to bed before 10.15 pm. Seventy-three patients (78.6%) reported an estimated bedtime between 10.15 pm and 00.30 am. Fifteen patients (16.2%) reported a bedtime after 00.30 am. Concerning waking up times: Thirty-two patients (34.4%) reported a waking up time between 05.00 am and 06.30 am. Twenty-two patients (24.7%) reported waking up between 06:30 and 07:45 am. Twenty-eight (30.1%) reported a time between 07:45 and 09:45 am. Finally, 10 patients (10.7%) reported a time after 09.45 am.

Relationship Between Sleep Quality and MASLD

The PSQI median score was higher in female patients when compared to male patients, and this difference was statistically significant (p=0.04). There was no significant difference in PSQI score in patients who had obesity, increased WC, DM, HT, HL, SAF activity score above 2, significant fibrosis, advanced fibrosis or severe MASLD compared to those who had not (Table 2).

Relationship Between Night eating Syndrome and MASLD

Thirty-one (33.3%) patients had night eating habits. There was no difference between genders. Furthermore, there was no significant difference in NEQ score in patients who had obesity, increased WC, DM, HT, and HL), SAF activity score above 2, significant fibrosis, advanced fibrosis, or severe MASLD compared to those who had not (Table 2).

Relationship Between Different Chronotype Preferences and MASLD

Concerning chronotypes, 48 (51.6%) patients were morning types, 3 (3.2%) were evening types, and 42 (45.2%) were neither types. Since the number of eveningness types is minimal, we compared the morningness and non-morningness groups. When we compare the two groups,

Table 1. Anthropometric and clinical characteristics of the participants

	Frequency (n=93)	%
Age (years), mean±SD		
Sex		67.7
Male	63	32.3
Female	30	
Obesity		32.3
Obese	30	67.7
Non-obese	63	
Waist circumference		22.6
Increased	21	77.4
Normal	72	
Diabetes		54.8
Diabetic	51	45.2
Non-diabetic	42	
Hypertension		38.7
Hypertansive	36	61.3
Non-hypertansive	57	
Hyperlipidemia		64.5
Hyperlipidemic	60	35.5
Non-hyperlipidemic	33	
SAF Steatosis Score		10.8
1	10	34.4
2	32	54.8
3	51	
SAF Activity Score		17.2
2	16	48.4
3	45	34.4
4	32	
SAF Fibrosis Score		6.5
0	6	29.0
1	27	31.2
2	29	26.9
3	25	6.5
4	6	
Moderate-to-severe steatosis		
S<2	10	10.8
S≥2	83	89.2
Severe activity		
A≥3	77	82.8
A<3	16	17.2
Significant fibrosis		
F<2	33	35.5
F≥2	60	64.5
Advanced fibrosis		
F<3	62	66.7
F≥3	31	33.3
Severe disease (A≥3 or F≥3)		
Severe	78	83.9
Non-severe	15	16.1
Psychometric measurements		
Pittsburg Sleep Quality Index (PSQI)		
Good sleepers (PSQI ≤5)	33	35.5
Poor sleepers (PSQI >5)	60	64.5
Morningness and Eveningness Questionnaire		
Morningness type	48	51.6
Neither-type	42	45.2
Eveningness type	3	3.2
Night Eating Questionnaire (NES)		
Night eating syndrome (NES≥18)	31	33.3
Non-night eating syndrome (NES<18)	62	66.7

SD: Standart deviation; SAF: Steatosis, activity, and fibrosis.

Table 2. Evaluation of sleep quality and night eating

	PSQI	p	NEQ	p
Age	5 (1–16)	0.17	14.79±6.29	0.24
Sex		0.04*		0.06
Male	5 (1–15)		14.00±6.49	
Female	6 (1–16)		16.46±5.58	
Obesity		0.50		0.36
Obese	5.5 (1–14)		15.66±6.48	
Non-obese	5 (1–16)		14.38±6.20	
Waist circumference		0.64		0.34
Increased	6 (2–16)		13.71±5.64	
Normal	5 (1–16)		15.11±6.47	
Diabetes		0.59		0.76
Diabetic	6 (1–15)		14.98±5.59	
Non-diabetic	5 (1–16)		14.57±7.11	
Hypertension		0.51		0.10
Hypertansive	6 (2–16)		16.13±6.28	
Non-hypertansive	5 (1–16)		13.94±6.20	
Hyperlipidemia		0.11		0.27
Hyperlipidemic	5 (1–16)		14.23±5.84	
Non-hyperlipidemic	7 (1–14)		15.81±7.01	
Moderate-to-severe steatosis		0.19		0.31
S<2	9 (2–16)		16.90±6.65	
S≥2	5 (1–16)		14.54±6.23	
Severe activity		0.86		0.90
A≥3	5 (1–16)		14.75±5.91	
A<3	5.5 (1–14)		15.00±8.09	
Significant fibrosis		0.22		0.95
F<2	6 (1–16)		14.84±7.24	
F≥2	5 (1–16)		14.76±5.76	
Advanced fibrosis		0.88		0.87
F<3	5 (1–16)		14.72±6.59	
F≥3	6 (2–15)		14.93±5.72	
Severe disease (A≥3 or F≥3)		0.81		0.72
Severe	5 (1–16)		14.66±5.92	
Non-severe	6 (1–14)		15.46±8.14	

*: P value <0.05 accepted as significant; PSQI: Pittsburg Sleep Quality Index; NEQ: Night Eating Questionnaire.

Table 3. Comparison of chronotype groups in MASLD and related clinical variables

	Mor. (n=49)	Non-mor. (n=48)	p
Age	48.77±8.25	44.44±11.00	0.04*
Sex			0.60
Male	33 (70.2%)	30 (65.2%)	
Female	14 (29.8%)	16 (34.8%)	
Obesity			0.60
Obese	14 (29.8%)	16 (34.8%)	
Non-obese	33 (70.2%)	30 (65.2%)	
Waist circumference			0.76
Increased	10 (21.3%)	11 (23.9%)	
Normal	37 (78.7%)	35 (76.1%)	
Diabetes			0.74
Diabetic	25 (53.2%)	26 (56.5%)	
Non-diabetic	22 (46.8%)	20 (43.5%)	
Hypertension			0.35
Hypertensive	16 (34.0%)	20 (43.5%)	
Non-hypertensive	31 (66.0%)	26 (56.5%)	
Hyperlipidemia			0.11
Hyperlipidemic	34 (72.3%)	26 (56.5%)	
Non-hyperlipidemic	13 (27.7%)	20 (43.5%)	
Moderate-to-severe steatosis			0.48
S<2	4 (8.5%)	6 (13.0%)	
S≥2	43 (91.5%)	40 (87.0%)	
Severe activity			0.25
A≥3	41 (87.2%)	36 (78.33%)	
A<3	6 (12.8%)	10 (21.7%)	
Significant fibrosis			0.46
F<2	15 (31.9%)	18 (39.1%)	
F≥2	32 (68.1%)	28 (60.9%)	
Advanced fibrosis			
F<3	30 (63.8%)	32 (69.6%)	0.55
F≥3	17 (36.2%)	14 (30.4%)	
Severe disease (A≥3 or F≥3)			0.14
Severe	42 (89.4%)	36 (78.3%)	
Non-severe	5 (10.6%)	10 (21.7%)	

*: P value <0.05 accepted as significant; Mor.: Morningness; Non-mor.: Non-morningness.

the age of the morningness group was higher than the non-morningness group, and this difference was statistically significant (p=0.04). The two groups revealed no significant difference according to obesity, increased WC, DM, HT, and HL), SAF activity score above 2, significant fibrosis, advanced fibrosis, or severe MASLD (Table 3).

Relationship Between Chronotype, Night Eating, Sleep Quality, MASLD, and Fibrosis

In patients with the morningness chronotype, 6 patients (29.0%) had NES, and in non-morningness patients, 22 patients (47.8%) had NES, which was significantly higher in non-morning patients (p=0.001). The median PSQI and mean NEQ scores were lower in the morningness group compared to the non-morningness group (p=0.002 and p<0.001, respectively). Finally, we examined whether there is a difference in disease severity between morning and non-morning chronotypes among those with night eating syndrome. We did not detect any statistically significant difference between the two groups. Regarding fibrosis, there was no difference in PSQI, night eating, and morningness-eveningness scores between significant and non-significant, also between advanced and non-advanced fibrosis groups.

In multivariate analysis, no variable was found that impacts moderate-to-severe steatosis, severe activity, significant fibrosis, and severe disease. On the other hand, age and poor sleep quality significantly impacted advanced fibrosis (OR: 1.11 and 3.81, respectively) (Table 4).

Table 4. The impact of parameters on advanced fibrosis in multivariate analysis

	Multivariable analysis (logistic regression)		
	Coef	**OR (95% CI)**	**p**
Age	0.105	1.11 (1.03–1.19)	0.005*
Poor sleep quality	1.340	3.81 (1.14–12.75)	0.029*

*: P value <0.05 accepted as significant; OR: Odd ratios; CI: Confidence interval.

Discussion

This cross-sectional study examined how chronotype differences and related night eating and sleep patterns affect MASLD severity. The first of the findings is that chronotype preferences did not differ between groups with different levels of disease severity and fibrosis. Second, however, we did not detect any significant relationship between sleep quality, night eating syndrome, and disease severity; the sleep quality was poorer, and night eating habits were more frequent in the non-morningness group than MASLD patients with morningness chronotype.

Despite many preclinical studies revealing the relationship between MASLD and circadian rhythm disruption, chronotype preference, an essential behavioral indicator of circadian rhythm phases, has not been adequately investigated in this population. To the extent of our knowledge, two studies examine the relationship between chronotype and MASLD.[8,13] In the previous study, researchers did not find a significant difference in chronotype scores between MASLD patients and healthy controls, and they did not reveal any relationship between disease severity and chronotype score, similar to our findings. However, this study has a small sample size (46 NAFLD patients) and did not present the number of individuals with chronotype preferences, provided evidence of poor sleep quality and shifts in food intake toward the night in MASLD patients, and reported that daytime sleepiness was correlated with the severity of fibrosis.[8] According to chronotype studies, approximately 40% of adults have one of the two extreme chronotypes; the rest is reported to be in the middle of the spectrum.[5] Therefore, taking a small sample in studies may have caused difficulties in identifying individuals with two opposite chronotypes and comparing them in terms of biological entities. The other study examined the relationship between disease severity and chronotype in patients with obesity. It showed that the eveningness chronotype was associated with more severe disease independently of age, gender, and BMI.[13] When we evaluate these findings with ours, it is striking that frequency of individuals with eveningness chronotype is significantly high (32.2%) in the study population compared to our study (3.1%). Research has shown a significant association between the eveningness chronotype and obesity.[14] Therefore, the difference in the frequency of chronotype in this study can be explained by the fact that the sample consisted of individuals with obesity. Similar to our research, in the previous study that did not find a relationship between MASLD and chronotype, BMI ratios were similar (29.8±7) to the mean BMI (32.2±4) in our research and significantly lower than the last study (45.6±6). Although the connection between chronotype and obesity, a key predictor of MASLD, has not been fully elucidated, it is accepted that chronotype-related genetic and behavioral factors contribute together to the formation of obesity.[15,16] Although nocturnal eating behavior, which can be seen as a behavioral indicator of chronotype typology[17] or independently, has been shown to be associated with weight gain,[18] there is not enough research on MASLD. In our study, although nocturnal eating habits were lower in people with morning-morning chronotype, we did not find a significant relationship between night-time eating habits and disease severity and related parameters. The lower prevalence of obesity and the small proportion of patients with extreme eveningness chronotype may contribute to the absence of a correlation between disease severity and chronotype in our study.

Contrary to chronotype studies, there are a significant number of studies investigating sleep quality and patterns in the MASLD population. However, there are few studies with null results, studies revealing the relationship between poor sleep quality and MASLD predominate.[19–24] In line with the previous research, we found that sleep quality was poor in patients with MASLD. Still, we did not find a significant relationship between sleep quality and the severity of MASLD and fibrosis. Considering the sleep characteristics and the determinants of sleep quality, two recent metanalyses indicated that short sleep duration was strongly correlated with an elevated risk of MASLD.[25,26] Several studies revealed that patients with MASLD have trouble getting up in the morning[7,27] and experience excessive daytime sleepiness.[25,28] Finally, later bedtime at night (after 1:00 am) was significantly associated with MASLD measured by liver ultrasound transient elastography.[29] When all these results are combined, we can hypothesize that decreased sleep duration and daytime sleepiness may also occur because of lifestyles incompatible with the chronobiological preferences (especially for eveningness) and endogenous circadian phases of the individuals, depending on work and social reasons. Clinical chronobiological studies with larger samples should clarify whether the poor sleep quality associated with MASLD is a primary cause or a mediator indicator. Our investigation determined that patients with non-morningness chronotype had worse sleep quality and more frequent night eating habits, supporting our hypothesis.

In addition, we observed that, despite the chronotype tendency of the population towards morningness, bedtimes are later than expected from morningness chronotype (93.8% reported a bedtime after 10.15 am) but waking up times are early (59.5% reported waking up time before 07.45 am). Although we did not assess daytime sleepiness, our results support the previous findings regarding short sleep duration in MASLD. Moreover, it may suggest that sleep times incompatible with chronotype preference may play a role in the etiology of MASLD.

Several limitations should be noted in our study. First, we did not include healthy participants without MASLD. The presence of a control group in the study could have provided more precise information on understanding the relationship between chronotype, sleep quality, nighttime eating habits, and disease severity. Second, we did not have a non-MASH MASLD group as our all patients were biopsy proven MASH. It would be better to compare the MASH with a non-MASH group in future studies to understand the differences about the topic between the two entities. Although we did not include people who received psychiatric treatments, considering that they may have a confounding effect on sleep quality and night eating behaviors, other medications used by the patients may have had a confounding effect on MASLD parameters. Since the number of people showing the evening chronotype is very limited in our population, we made comparisons between the groups with and without morningness chronotypes. Although it is stated in chronotype studies that individuals' chronotype preference should be evaluated in a spectrum between extreme morningness and extreme eveningness,[30] the fact that we made the comparisons between groups that are close to each other instead of two opposite biological ends of the spectrum may have affected the results of our research. Finally, considering the relationship between the mean sleep and wake times of

our sample and later bedtimes, it can be thought that our sample has a lifestyle that does not show a significant deviation from its circadian rhythm but a delayed sleep time. Whether chrono disruption due to this deviation will increase MASLD may be a subject of investigation. Due to the natural frequency of chronotype distribution in adults, instead of comparing the small number of evening and morning chronotypes in the limited sample group, detecting individuals with extreme chronotypes by chronotype screening and comparing these individuals in terms of MASLD data may provide more accurate information. We recommend future studies compare individuals with extreme chronotypes and evaluate the possible effects of circadian misalignment.

Conclusion

Preclinical studies emphasize the importance of circadian disruption in the etiology of MASLD, but studies examining the relationship between chronotype and MASLD in clinical samples are needed. Recognition of the modifiable risk factors mediating the etiology and progression of MASLD and understanding the role of chronobiology in this process may provide a basis for simple and low-cost treatment methods such as bright light therapy providing circadian regulation to take place in the treatment of MASLD.

Ethics Committee Approval: The Marmara University Clinical Research Ethics Committee granted approval for this study (date: 05.04.2019, number: 09.2019.370).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – ASK, YY; Design – ASK, YY; Supervision – YY; Materials – AO, HTK; Data Collection and/or Processing – AO, HTK; Analysis and/or Interpretation – HTK; Literature Search – ASK; Writing – ASK, YY; Critical Reviews – KS, YY, FE.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multi-society Delphi consensus statement on new fatty liver disease nomenclature. J Hepatol 2023:101133. doi: 10.1016/j.jhep.2023.06.003. [Epub ahead of print]. [CrossRef]
2. Guo X, Yin X, Liu Z, Wang J. Non-alcoholic fatty liver disease (NAFLD) pathogenesis and natural products for prevention and treatment. Int J Mol Sci 2022;23(24):15489. [CrossRef]
3. Shetty A, Hsu JW, Manka PP, Syn WK. Role of the circadian clock in the metabolic syndrome and nonalcoholic fatty liver disease. Dig Dis Sci 2018;63(12):3187-3206. [CrossRef]
4. Marjot T, Ray DW, Tomlinson JW. Is it time for chronopharmacology in NASH? J Hepatol 2022;76(5):1215-1224. [CrossRef]
5. Kandeğer A, Eğilmez Ü, Selvi Y. Feeding and eating disorders in the context of circadian rhythms. Alpha Psychiatry 2021;22(6):278-284. [CrossRef]
6. Selvi Y, Beşiroğlu L, Aydın A. Chronobiology and mood disorders. Current Approaches in Psychiatry 2011;3(3):368-386. [Turkish] [CrossRef]
7. Zarean E, Looha MA, Amini P, Ahmadi A, Dugué PA. Sleep characteristics of middle-aged adults with non-alcoholic fatty liver disease: findings from the Shahrekord PERSIAN cohort study. BMC Public Health 2023;23(1):312.
8. Bernsmeier C, Weisskopf DM, Pflueger MO, Mosimann J, Campana B, Terracciano L, 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(11):e0143293.
9. Nascimbeni F, Bedossa P, Fedchuk L, Pais R, Charlotte F, Lebray P, et al. Clinical validation of the FLIP algorithm and the SAF score in patients with non-alcoholic fatty liver disease. J Hepatol 2020;72(5):828-838. [CrossRef]
10. Agargun MY, Cilli AS, Boysan M, Selvi Y, Gulec M, Kara H. Turkish version of morningness-eveningness questionnaire (MEQ). Sleep Hypn 2007;9(1):16.
11. Buysse DJ, Reynolds III CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28(2):193-213. [CrossRef]
12. Atasoy N, Saracli O, Konuk N, Ankarali H, Guriz S, Akdemir A, et al. The reliability and validity of Turkish version of The Night Eating Questionnaire in psychiatric outpatient population. Anatol J Psychiatry 2014;15(3):238-247. [Turkish] [CrossRef]
13. Vetrani C, Barrea L, Verde L, Sarno G, Docimo A, de Alteriis G, et al. Evening chronotype is associated with severe NAFLD in obesity. Int J Obes (Lond) 2022;46(9):1638-1643. [CrossRef]
14. Teixeira GP, Guimarães KC, Soares A, Marqueze EC, Moreno CRC, Mota MC, et al. Role of chronotype in dietary intake, meal timing, and obesity: a systematic review. Nutr Rev 2022;81(1):75-90. [CrossRef]
15. De Amicis R, Galasso L, Leone A, Vignati L, De Carlo G, Foppiani A, et al. Is abdominal fat distribution associated with chronotype in adults independently of lifestyle factors? Nutrients 2020;12(3):592. [CrossRef]
16. Ruiz-Lozano T, Vidal J, de Hollanda A, Canteras M, Garaulet M, Izquierdo-Pulido M. Evening chronotype associates with obesity in severely obese subjects: interaction with CLOCK 3111T/C. Int J Obes (Lond) 2016;40(10):1550-1557.
17. van der Merwe C, Münch M, Kruger R. Chronotype differences in body composition, dietary intake and eating behavior outcomes: A scoping systematic review. Adv Nutr 2022;13(6):2357-2405. [CrossRef]
18. Allison KC, Goel N, Ahima RS. Delayed timing of eating: Impact on weight and metabolism. Curr Obes Rep 2014;3(1):91-100. [CrossRef]
19. Liu H, Huang S, Xu M, Zhao D, Wang X, Zhang L, et al. The association between sleep duration, quality, and nonalcoholic fatty liver disease: A cross-sectional study. Open Med (Wars) 2023;18(1):20230670. [CrossRef]
20. Okamura T, Hashimoto Y, Hamaguchi M, Obora A, Kojima T, Fukui M. Short sleep duration is a risk of incident nonalcoholic fatty liver disease: a population-based longitudinal study. J Gastrointestin Liver Dis 2019;28(1):73-81.
21. Marin-Alejandre BA, Abete I, Cantero I, Riezu-Boj JI, Milagro FI, Monreal JI, et al. Association between sleep disturbances and liver status in obese subjects with nonalcoholic fatty liver disease: A comparison with healthy controls. Nutrients 2019;11(2):322. [CrossRef]
22. Takahashi A, Anzai Y, Kuroda M, Kokubun M, Kondo Y, Ogata T, et al. Effects of sleep quality on non-alcoholic fatty liver disease: a cross-sectional survey. BMJ Open 2020;10(10):e039947. [CrossRef]
23. Um YJ, Chang Y, Jung HS, Cho IY, Shin JH, Shin H, et al. Decrease in sleep duration and poor sleep quality over time is associated with an increased risk of incident non-alcoholic fatty liver disease. J Pers Med 2022;12(1):92. [CrossRef]
24. Kim CW, Yun KE, Jung HS, Chang Y, Choi ES, Kwon MJ, 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(2):351-357. [CrossRef]
25. Wijarnpreecha K, Thongprayoon C, Panjawatanan P, Ungprasert P. Short sleep duration and risk of nonalcoholic fatty liver disease: A systematic review and meta-analysis. J Gastroenterol Hepatol 2016;31(11):1802-1807. [CrossRef]
26. Yang J, Zhang K, Xi Z, Ma Y, Shao C, Wang W, et al. Short sleep duration and the risk of nonalcoholic fatty liver disease/metabolic associated fatty liver disease: a systematic review and meta-analysis. Sleep Breath. 2022:1-12. doi: 10.1007/s11325-022-02767-z. [Epub ahead of print]. [CrossRef]
27. Fan H, Liu Z, Zhang X, Yuan H, Zhao X, Zhao R, et al. Investigating the association between seven sleep traits and nonalcoholic fatty liver disease: Observational and mendelian randomization study. Front Genet 2022;13:792558. [CrossRef]
28. Yu L, Lin C, Chen X, Teng Y, Zhou S, Liang Y. A meta-analysis of sleep disorders and nonalcoholic fatty liver disease: potential causality and symptom management. Gastroenterol Nurs 2022;45(5):354-363. [CrossRef]
29. Zhou J, Long Y, Ding N, Su Y. Association between bedtime at night and nonalcoholic fatty liver disease diagnosed by liver ultrasound transient elastography. Diabetes Res Clin Pract 2022;184:10919530. [CrossRef]
30. Natale V, Cicogna P. Morningness-eveningness dimension: is it really a continuum? Pers Individ Differ 2002;32(5):809-816. [CrossRef]