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Association Between Gastrointestinal Symptoms and Sleep Habits in Children with Metabolic Dysfunction-Associated Steatotic Liver Disease: A Cross-Sectional Study

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ABSTRACT

Objective: Reduced sleep quality in children has been associated with obesity and fatty liver disease. However, there are no studies evaluating the impact of gastrointestinal symptoms on sleep quality in children with metabolic dysfunction-associated steatotic liver disease (MASLD). The aim of this cross-sectional study was to investigate the prevalence of gastrointestinal symptoms and sleep disturbances in children with MASLD and to examine the association of gastrointestinal symptoms with sleep disturbances.

Methods: Anthropometric and biochemical examinations were performed on children aged 8-18 years, including children with MASLD and matched healthy controls for comparison. The Hepatic Steatosis Index (HSI) and Non-Alcoholic Fatty Liver Disease Fibrosis Score (NFS) were calculated for children with MASLD. Sleep disturbances were assessed using the Child Sleep Habits Questionnaire (CSHQ), and gastrointestinal symptoms were assessed using the Gastrointestinal Symptom Rating Scale (GSRS). Logistic regressions were used to examine factors associated with sleep quality.

Results: A total of 176 children, consisting of 84 (47.7%) with MASLD and 92 healthy controls were included. Of these 123 (69.9%) had sleep disturbances. In unadjusted analysis, sleep disturbances were significantly more common in the MASLD group (89% vs 57%, $p < 0.001$). However, in the final multivariate regression model adjusting for metabolic confounders, the independent predictors of sleep disturbances were low family income [odds ratio (OR)=9.56, 95% confidence interval (CI)=2.80-32.57], total GSRS score (OR=1.15, 95% CI=1.06-1.24), and Homeostatic

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Model Assessment of Insulin Resistance (OR=1.51, 95% CI=1.01-2.27). The presence of MASLD lost statistical significance after adjustment ($p=0.554$). NFS, a marker of fibrosis risk, was associated with both sleep disturbances and gastrointestinal symptoms.

Conclusion: This study showed that sleep disturbances and gastrointestinal symptoms are more common in children with MASLD, and that gastrointestinal disturbances are significantly associated with sleep disturbances. Furthermore, the results suggest that sleep disturbances may be more common in children with MASLD who have a higher estimated risk of liver fibrosis. Children with MASLD should be evaluated not only for liver health but also for extrahepatic conditions, including sleep and gastrointestinal disorders.

Keywords: Children, gastrointestinal symptoms, metabolic dysfunction-associated fatty liver disease, obesity, sleep quality

What is already known on this topic?

Gastrointestinal disorders and sleep disorders are more common in obese individuals than in the normal population. Some children with obesity will develop metabolic dysfunction-associated steatotic liver disease (MASLD).

What this study adds?

This study demonstrated a high prevalence of sleep disturbances and gastrointestinal symptoms in children with MASLD. Gastrointestinal symptoms contributed to sleep disturbances in children with MASLD. Liver fibrosis risk was associated with sleep disturbances, particularly sleep anxiety and sleep duration.

Introduction

Sleep, a vital component of quality of life, plays a critical role in children's physical growth, neurological development, and behavioral maturation (1). Sleep disorders in children may lead to numerous issues, including daytime sleepiness, diminished neurocognitive performance, and poor academic achievement (2). It is estimated that 10-20% of children experience sleep disorders severe enough to require medical intervention (3). Obese children are at higher risk of developing sleep disorders, particularly obstructive sleep apnea (4,5). Obesity also exerts both direct and indirect effects on gastrointestinal functions. In these individuals, central adiposity increases intra-abdominal pressure, contributing to a wide range of problems that may include gastroesophageal reflux and gallstone formation because of metabolic dyslipidemia (6). Moreover, in obese individuals with metabolic dysfunction-associated steatotic liver disease (MASLD), alterations in proinflammatory adipokine and cytokine release, disruption of the liver-brain-gut neural axis and gut-liver crosstalk, and changes in gut microbiota are frequently associated with functional disorders, like irritable bowel syndrome (7).

Insufficient sleep, delayed sleep onset, and poor sleep quality are common in adults with functional gastrointestinal disorders (8). Similarly, children with functional gastrointestinal disorders also exhibit prevalent sleep disturbances, and those with sleep problems report more severe abdominal pain (9). In obese adults, gastrointestinal symptoms have been shown to correlate with sleep disorders (10). However, no studies have

investigated the relationship between sleep disturbances and gastrointestinal symptoms in children with MASLD. To address this, the aims of the present study were: (i) to determine the frequency of gastrointestinal symptoms and prevalence of sleep disorders in children with MASLD, (ii) to examine the association between gastrointestinal symptoms and sleep disturbances in this population, and (iii) to investigate if and how hepatic steatosis severity correlated with both sleep problems and gastrointestinal symptoms.

Methods

Study Design and Ethical Aspects

This study was a cross-sectional, analytical investigation with a control group. The research was conducted among overweight or obese children and adolescents aged 8-18 years and a healthy sex and age-matched control group with a normal body mass index (BMI), no known disease, normal liver function tests and liver ultrasound (US). The study protocol was approved by the Antalya Training and Research Hospital Scientific Ethics Committee for Medical Research (date: 05.12.2024, approval no.: 19/21) prior to commencement. Written and verbal informed consent was obtained from both participating children and their parents prior to enrollment. The study was conducted in accordance with the Declaration of Helsinki regarding human and animal rights and local laws and regulations.

Participants

The study included overweight or obese children and adolescents aged 8-18 years who were referred to our

department with suspected liver disease. Based on the most recent NAFLD Nomenclature consensus group guidelines (11), patients were divided into two groups, those with MASLD and those without MASLD, using laboratory and ultrasound findings as sub-group inclusion criteria. Children were excluded from study participation if they had an infectious or autoimmune liver diseases (hepatitis A, B, C, infectious mononucleosis, autoimmune hepatitis), metabolic liver diseases (Wilson's disease, alpha-1 antitrypsin deficiency, cystic fibrosis), other chronic conditions (e.g., bronchial asthma, chronic renal failure, oncologic diseases), endocrine-related obesity (hypercortisolism, hypopituitarism, hypothyroidism, hypothalamic-pituitary injury), medications and substance use (use of medications that affect body weight, blood pressure, or metabolism, such as glucocorticoids, psychiatric medications, anticonvulsants-smoking and/or alcohol consumption), and refusal to provide informed consent by parents and/or patients over 16 years of age. The control group consisted of age- and sex-matched children who were examined at the same hospital's pediatric outpatient clinics for mild physical symptoms, such as a common cold, rhinitis and had no chronic medical or psychiatric conditions.

Socio-demographic Data Form

This form was designed to collect socio-demographic information about the children and their families. The form included details such as, participants' age, gender, family's monthly income and parental education levels.

Anthropometric Measurements

Measurements of body weight and height were taken when the children were wearing light clothing and were barefoot. BMI was calculated using the standard formula: weight (kg)/ height² (m). According to the World Health Organization, overweight was defined as BMI standard deviation score (SDS) >1, and obesity as BMI SDS >2 (12).

Liver Ultrasonography

Routine B-mode US investigation was performed by a single radiologist with more than 10 years of experience in US imaging. US images of the liver were obtained using subcostal and intercostal planes. The requested fasting time was 6 hours. Hepatic steatosis was diagnosed based on known US characteristics, including increased parenchymal echogenicity, hepatorenal echo contrast, impaired visualization of the diaphragm line and intrahepatic portal vein wall, and deep attenuation of the liver parenchyma (13).

Biochemical Analyses

Blood samples were collected from participants after a 12-hours overnight fast. Routine biochemical analyses including alanine aminotransferase (ALT), aspartate aminotransferase (AST),

gamma glutamyltransferase (GGT), albumin, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, glucose and insulin, all of which were measured by standard clinical laboratory techniques. The homeostasis model assessment of insulin resistance [HOMA-IR=insulin (mU/L) glucose (mmol/L)/22.5] was calculated using serum concentrations of glucose and insulin (14).

Hepatic Indexes

Different indirect hepatic markers were calculated by taking into account the necessary criteria and applying accepted formulas (15). The Hepatic Steatosis Index (HSI) and Non-Alcoholic Fatty Liver Disease Fibrosis Score (NFS) were chosen as proxy markers for hepatic steatosis in this population (16). The HSI was obtained using the established formulas and includes the ALT/AST ratio, BMI, presence of diabetes mellitus and sex, and was developed to detect hepatic steatosis. The NFS identifies individuals at risk for significant liver fibrosis due to steatosis using factors such as age, BMI, presence of diabetes, AST/ALT ratio, platelet count, and albumin, again using the established formula. These indices were selected as they reflect different aspects of MASLD: the HSI primarily estimates the degree of hepatic steatosis, while the NFS estimates the risk of associated fibrosis, incorporating broader metabolic factors.

Gastrointestinal Symptom Rating Scale (GSRS)

The GSRS is a measurement tool used to assess gastrointestinal symptoms in individuals, originally developed by Revicki et al. (17) in 1998. Its validity and reliability for the Turkish population were established by Turan et al. (18) in 2017, confirming its applicability. The scale consists of 15 items scored on a 7-point Likert scale (ranging from "no discomfort" to "very severe discomfort") and is divided into five subdomains: reflux (items 2 and 3), abdominal pain (items 1,4, and 5), indigestion (items 6,7,8, and 9), diarrhea (items 11,12, and 14), and constipation (items 10,13, and 15). Each item evaluates the patient's self-reported gastrointestinal symptoms over the past week. The total score ranges from 0 to 105, with higher scores indicating more severe gastrointestinal symptoms. In the adaptation study, the scale demonstrated high internal consistency, with a Cronbach's alpha coefficient of 0.82 (18).

Child Sleep Habits Questionnaire (CSHQ)

This questionnaire was originally developed by Owens et al. (19) in 2000 as a 45-item tool, with a subsequent short form consisting of 33 functional items. Its Turkish adaptation has been validated, demonstrating a Cronbach's alpha coefficient of 0.78 (20). The CSHQ comprises eight subscales: bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night wakings, parasomnias, sleep-disordered breathing, and daytime sleepiness. Parents retrospectively evaluate their child's sleep

patterns over the past week. Items are scored on a 3-point scale: usually (behavior occurring 5-7 times/week)=3, sometimes (2-4 times/week)=2, and rarely (never or once weekly)=1. Six items are reverse-scored. The clinical cutoff is set at 41 points, with higher scores indicating clinically significant sleep problems, while a total score ≤ 41 suggests no significant sleep disturbances.

Sample Size

G Power software version 3.1.9.7, was used with an alpha of 0.05 (two-sided) and 95% power. We calculated the sample size based on the mean difference between two independent groups (obese group and healthy). The means and standard deviations of sleep problems in children were taken from an earlier similar study (obesity case 43.62 ± 8.26 , healthy control 39.89 ± 5.19) (21) as we used the CSHQ in this earlier research. The required sample size was a minimum of 82 participants in each group.

Statistical Analysis

Statistical evaluations were made using Statistical Package for the Social Sciences (SPSS) for Windows, version 26.0 (IBM Corp., Armonk, New York, USA). The normality of the distribution was evaluated by the Kolmogorov-Smirnov test. To compare the data obtained from the MASLD groups and control groups who participated in the study, the independent sample t-test was used for normally distributed data and the Mann-Whitney U test was used for non-normally distributed data. Categorical data were compared using the chi-square test. Descriptive statistical values including mean and standard deviation were derived for continuous data, and median and interquartile range (IQR) were calculated for non-parametric data. To evaluate the relationship between the sociodemographic data and scale scores of the MASLD groups and controls, Pearson's correlation analysis was used for parametric data, and Spearman's correlation analysis was used for non-parametric data. The association between several factors and sleep disturbance was investigated using logistic regression after adjusting for confounding factors, then analyzed using three models. Model 1 was adjusted for demographic characteristics (gender, age, family income status) and key metabolic confounders (BMI SDS and HOMA-IR score). Model 2 was adjusted for all variables in Model 1 plus the presence of MASLD. Model 3 was adjusted for all variables in Model 2 plus the total GSRS score.

Results

A total of 176 participants, including 84 (47.7%) children with MASLD and 92 healthy control, who presented to the Antalya Training and Research Hospital, Clinic of Pediatric Gastroenterology between 01 January 2025 and 30 August, 2025, were included in the study (Figure 1).

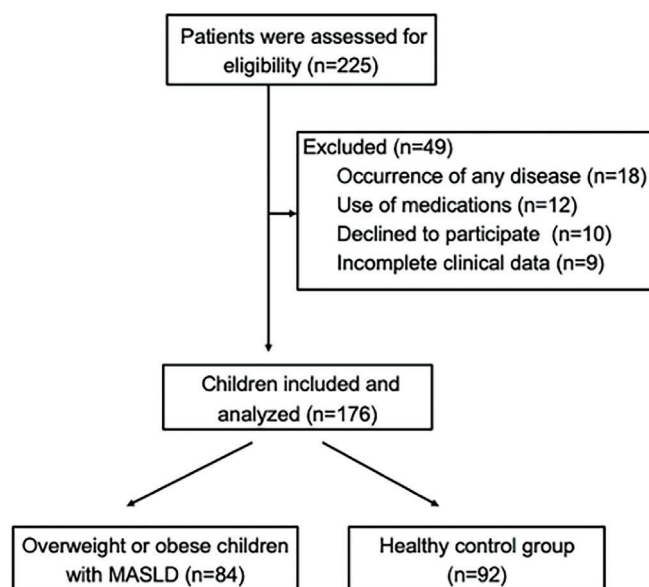


Figure 1. Number of children evaluated for enrollment, included in the study, and excluded

Characteristics of Participants

The participants' demographic characteristics, anthropometric measurements, and laboratory parameters are shown in Table 1. The median age of the children in the study was 13.5 years (Range 8-18 years), and 47.2% were girls. There was no significant difference between the MASLD and control groups in terms of age, gender, education level, marital status of parents or family income status ($p > 0.05$). Laboratory parameters including ALT (14.0 vs. 30.0, $p < 0.001$), AST (20.0 vs. 27.0, $p < 0.001$), GGT (13.0 vs. 24.0, $p < 0.001$), ALP (125.0 vs. 161.0, $p = 0.005$), HOMA-IR (1.37 vs. 3.48, $p < 0.001$), and triglyceride (70.0 vs. 103.0, $p < 0.001$) levels were higher in children with MASLD.

A Comparison of Scales Between the Children with MASLD and Control Groups

Children with MASLD demonstrated significantly higher total GSRS scores compared to the healthy controls [$p = 0.001$, odds ratio (OR)=1.081]. Based on GSRS results (Table 2), symptoms of reflux, abdominal pain, indigestion, diarrhea, and constipation were all significantly more prevalent in the MASLD group. Table 2 also shows a comparison of the CSHQ scores between the children with MASLD and the control groups. The CSHQ scores revealed that the total scale score ($p < 0.001$, OR=1.111), along with the subscale scores for bedtime resistance, sleep duration, sleep anxiety, night waking, parasomnias, and sleep-disordered breathing, were all statistically significantly worse in children with MASLD.

A total of 123 participants (69.9%) had clinically significant sleep disturbances according to the CSHQ. Sleep disturbances were present in 75 children (89.3%) with MASLD, compared to 48 children (52.2%) in the control group ($p<0.001$).

Factors Associated with Sleep Disturbances

The relationship between potential risk factors and sleep disturbances was re-evaluated using multivariable logistic regression to adjust for key metabolic confounders, including BMI SDS and HOMA-IR. The results of the adjusted analyses are presented in Table 3. In the initial model adjusted for demographic and metabolic factors only (Model 1), low family income [adjusted OR (aOR)=6.72, 95% CI 2.19-20.62, $p=0.001$] and higher BMI SDS (aOR=1.59, 95% CI 1.11-2.28, $p=0.011$) were significantly associated with sleep disturbances. When MASLD status was added to the model (Model 2), low family

income remained a strong predictor (aOR=6.87, 95% CI 2.24-21.01, $p=0.001$), but the presence of MASLD itself was not statistically significant (aOR=3.67, 95% CI 0.55-24.58, $p=0.181$). In the final, fully adjusted model (Model 3), which also included gastrointestinal symptom severity, low family income (aOR=9.56, 95% CI 2.80-32.57, $p<0.001$), higher GSRS total score (aOR=1.15 per point, 95% CI 1.06-1.24, $p<0.001$), and higher HOMA-IR (aOR=1.51, 95% CI 1.01-2.27, $p=0.045$) emerged as independent factors associated with sleep disturbances. The presence of MASLD was not a significant predictor in this model (aOR=0.51, 95% CI 0.05-4.81, $p=0.554$).

Correlation Between Digestive Symptoms and Sleep Disturbances in Children with MASLD

The analysis revealed distinct correlation patterns between the symptom scales and liver disease indices. No correlation was

Table 1. Socio-demographics characteristics and laboratory parameters children with MASLD and healthy controls

Parameters	Healthy controls (n=92)	Children with MASLD (n=84)	p value
Gender, female, n (%)	44 (47.8%)	39 (46.4%)	0.881
Age, years, mean±SD	13.3±2.5	13.7±2.6	0.813
Child's schooling status, n (%)			
Primary school	22 (23.9)	15 (17.9)	0.398
Secondary school	44 (47.8)	38 (45.2)	
High school	26 (28.3)	31 (36.9)	
Marital status of parents, n (%)			
Married	82 (89.1)	76 (90.5)	0.768
Divorced	10 (10.9)	8 (9.5)	
Family income status, n (%)			
Good	10 (10.9)	9 (10.7)	0.811
Average	54 (58.7)	53 (63.1)	
Poor	28 (30.4)	22 (26.2)	
BMI, kg/m², mean±SD	19.8±3.3	32.7±6.1	<0.001*
BMI z score, median (IQR)	0.07 (-0.83-0.58)	2.85 (2.39-3.25)	<0.001*
ALT, U/L, median (IQR)	14.0 (11.0-17.0)	30.0 (21.0-54.75)	<0.001*
AST, U/L, median (IQR)	20.0 (16.0-23.0)	27.0 (20.0-36.75)	<0.001*
GGT, U/L, median (IQR)	13.0 (11.0-16.0)	24.0 (18.0-32.25)	<0.001*
ALP, U/L, median (IQR)	125.0 (98.0-184.0)	161.0 (104.0-249.0)	0.005*
Albumin, g/dL, mean±SD	4.3±0.5	4.1±0.4	0.265
Total cholesterol, mg/dL, mean±SD	138.1±28.9	153.3±33.8	0.001*
Triglyceride, mg/dL, median (IQR)	70.0 (59.5-90.0)	103.0 (77.7-150.5)	<0.001*
HDL cholesterol, mg/dL, mean±SD	55.1±10.8	44.5±11.0	<0.001*
LDL cholesterol, mg/dL, mean±SD	77.7±21.8	88.0±26.8	0.006*
HOMA-IR, median (IQR)	1.37 (1.10-1.92)	3.48 (2.60-6.05)	<0.001*

*Statistically significant

BMI: body mass index, ALT: alanine aminotransferase, AST: aspartate aminotransferase, GGT: gamma glutamyltransferase, ALP: alkaline phosphatase, HDL: high-density lipoprotein, LDL: low-density lipoprotein, HOMA-IR: homeostasis model assessment-estimated insulin resistance, MASLD: metabolic dysfunction-associated steatotic liver disease, SD: standard deviation, IQR: interquartile range.

Table 2. A comparison of gastrointestinal symptom rating scale and child sleep habits questionnaire scores between the children with MASLD and healthy controls

	Children with MASLD (n=84)	Healthy controls (n=92)	Odds ratio	95% Confidence interval	p value
CSHQ, mean (SD)					
Bedtime resistance	10.8 (2.7)	9.6 (2.5)	1.190	1.059-1.338	0.003*
Sleep-onset delay	1.8 (0.8)	1.6 (1.3)	-	-	0.217
Sleep duration	5.4 (1.8)	4.3 (1.2)	1.364	1.149-1.618	0.001*
Sleep anxiety	6.3 (1.7)	5.1 (1.9)	1.327	1.129-1.561	<0.001*
Night wakings	4.7 (1.4)	3.8 (1.1)	1.603	1.259-2.041	<0.001*
Parasomnias	11.3 (3.1)	8.6 (2.4)	1.404	1.221-1.616	<0.001*
Sleep-disordered breathing	5.0 (1.4)	3.5 (1.2)	1.672	1.344-2.081	<0.001*
Total score	54.9 (10.7)	43.8 (10.1)	1.111	1.071-1.153	<0.001*
GSRS, mean (SD)					
Reflux	3.9 (1.2)	2.9 (0.9)	1.209	1.046-1.397	0.004*
Abdominal pain	7.6 (2.2)	5.1 (1.6)	1.238	1.120-1.369	0.001*
Indigestion	9.7 (2.3)	6.5 (2.1)	1.174	1.085-1.271	0.003*
Diarrhea	6.4 (1.9)	3.8 (1.1)	1.479	1.239-1.765	<0.001*
Constipation	5.9 (1.8)	4.3 (1.3)	1.215	1.078-1.370	0.001*
Total score	33.6 (9.6)	22.6 (6.2)	1.081	1.047-1.115	0.001*

*Statistically significant
CSHQ: child sleep habits questionnaire, GSRS: gastrointestinal symptom rating scale, MASLD: metabolic dysfunction-associated steatotic liver disease, SD: standard deviation

Table 3. Logistic regression analysis of factors associated with sleep disturbances in children

Variable	Model 1 aOR (95% CI)	p value	Model 2 aOR (95% CI)	p value	Model 3 aOR (95% CI)	p value
Age	1.024 (0.867-1.209)	0.782	1.022 (0.863-1.209)	0.804	0.974 (0.804-1.178)	0.783
Gender (Male)	0.896 (0.379-2.116)	0.802	0.999 (0.414-2.410)	0.997	1.120 (0.407-3.082)	0.826
Family Income (Low)	6.721 (2.191-20.620)	0.001	6.867 (2.244-21.012)	0.001	9.555 (2.803-32.569)	<0.001
BMI z-score	1.591 (1.112-2.277)	0.011	1.142 (0.628-2.078)	0.664	1.602 (0.791-3.244)	0.191
HOMA-IR	1.446 (0.998-2.096)	0.051	1.350 (0.931-1.956)	0.114	1.514 (1.010-2.271)	0.045
MASLD (Presence)	-	-	3.665 (0.547-24.580)	0.181	0.507 (0.053-4.812)	0.554
GSRS Total Score	-	-	-	-	1.146 (1.063-1.236)	<0.001

Model 1: Adjusted for age, gender, family income, BMI z-score, and HOMA-IR
Model 2: Adjusted for all variables in Model 1 plus the presence of MASLD
Model 3: Adjusted for all variables in Model 2 plus the total gastrointestinal symptom rating scale (GSRS) score
aOR: adjusted odds ratio, CI: confidence interval, MASLD: metabolic dysfunction-associated steatotic liver disease, GSRS: gastrointestinal symptom rating scale

found between the total GSRS score and the HSI, and among the GSRS subgroups, only reflux showed a significant link to HSI. Similarly, the total CSHQ score was not correlated with HSI, with only its sleep-onset delay and sleep duration subscales demonstrating a significant, albeit weak, relationship. In contrast, while the total GSRS and total CSHQ scores also showed no correlation with the NFS, specific subscales suggest a different story. For NFS, positive correlations were identified with the GSRS subgroups of reflux and diarrhea. Furthermore, a broad range of sleep issues were associated with NFS, including bedtime resistance, sleep-onset delay, sleep duration, sleep anxiety, night wakings, and parasomnias. The strength of these correlations

was mostly weak, except for the relationships between NFS and both sleep duration and sleep anxiety, which were of moderate strength (Table 4).

Discussion

The results of our study suggest that children with MASLD had a higher prevalence of sleep disturbances and gastrointestinal symptoms compared to healthy children. However, after adjusting for key metabolic confounders, including BMI and HOMA-IR, the strongest independent risk factors for sleep disturbance were low family income, increased gastrointestinal

Table 4. Correlation between hepatic steatosis index and NAFLD fibrosis score with CSHQ and GSRS scores in children with MASLD

	Hepatic steatosis index		NAFLD fibrosis score	
	r	p value	r	p value
CSHQ				
Bedtime resistance	0.035	0.374	0.220	0.025*
Sleep-onset delay	0.211	0.027*	0.210	0.031*
Sleep duration	0.250	0.011*	0.301	0.003*
Sleep anxiety	0.103	0.177	0.361	<0.001*
Night wakings	0.074	0.250	0.208	0.032*
Parasomnias	0.013	0.453	0.247	0.014*
Sleep-disordered breathing	0.017	0.438	0.016	0.446
Total score	0.081	0.233	0.097	0.196
GSRS				
Reflux	0.260	<0.008*	0.291	0.004*
Abdominal pain	0.046	0.339	0.017	0.440
Indigestion	0.008	0.472	0.144	0.101
Diarrhea	0.154	0.081	0.204	0.034*
Constipation	0.003	0.489	0.000	0.997
Total score	0.042	0.351	0.110	0.166
Data are presented as Spearman's correlation coefficient (r _s) and corresponding p values				
*Statistically significant				
CSHQ: child sleep habits questionnaire, GSRS: gastrointestinal symptom rating scale, MASLD: metabolic dysfunction-associated steatotic liver disease				

symptom severity, and higher HOMA-IR. NFS, which reflects liver fibrosis risk, was significantly associated with multiple subdimensions of both sleep disturbances and gastrointestinal symptoms in children with MASLD, whereas the relationships with the HSI were more limited. Our findings demonstrate that the clinical implication of MASLD extends beyond the liver and is intertwined with sleep and gastrointestinal health, with these extra-hepatic manifestations being more strongly linked to underlying metabolic dysfunction and socioeconomic factors than to the hepatic diagnosis alone.

A meta-analysis by Yu et al. (22) reported that individuals with NAFLD commonly experience sleep disorders, primarily short sleep duration. A recent large-scale study also identified a strong association between sleep disorders and MASLD (23). In line with these reports, we observed a strong unadjusted association between MASLD and sleep disturbances. However, after adjustment for BMI and HOMA-IR, this association was attenuated and lost statistical independence. This suggests that the link between MASLD and poor sleep may be largely mediated by the underlying obesity and insulin resistance that characterize MASLD, rather than hepatic steatosis per se. Although not directly measured in our study, the pro-inflammatory state and gut

dysbiosis associated with obesity and insulin resistance (24) are known to enhance systemic cytokines (TNF- α , IL-1 β , IL-6), which may cross the blood-brain barrier, trigger neuroinflammation, and potentially disrupt sleep-regulating pathways (25,26).

A key finding from our adjusted analysis (Model 3) was that low family income, gastrointestinal symptom severity (GSRS score), and HOMA-IR each emerged as independent risk factors for sleep disturbance. The strong and independent association of the gastrointestinal symptom score with sleep problems suggests a potential direct link between gut discomfort and sleep disturbance in children, irrespective of a MASLD diagnosis. Gastrointestinal discomfort, particularly reflux, is common in individuals with MASLD and obesity (7,27). Symptoms such as nocturnal reflux, abdominal pain, or bloating can directly interrupt sleep, prolong sleep onset latency, and reduce sleep depth. The significantly higher "night wakings" and "sleep onset delay" subscale scores in our MASLD group support this mechanism. Furthermore, increased gastrointestinal symptoms and chronic abdominal discomfort are thought to be associated with a shift toward sympathetic dominance in the autonomic nervous system (28). Although we did not assess autonomic function, such a shift, if present, could theoretically exacerbate symptoms and simultaneously suppress parasympathetic activity, which is crucial for initiating and maintaining sleep, thereby potentially contributing to sleep disorders (29).

The persistent and strong association between low family income and sleep disturbances across all our regression models underscores the profound influence of socioeconomic status as a key social determinant of health. This relationship likely operates through multiple interconnected pathways. Firstly, financial strain can create a chronically stressful home environment, elevating hormones responsive to stress, like cortisol, that disrupt circadian rhythms and sleep architecture. Secondly, socioeconomic constraints often translate into suboptimal sleep conditions, including crowded living spaces, noise pollution, and lack of a consistent bedtime routine. Thirdly, lower income is frequently associated with poorer dietary quality, characterized by high consumption of processed foods, which can negatively impact both sleep quality and MASLD progression. Therefore, low family income should not be viewed merely as a demographic variable but as a marker of broader environmental and psychosocial adversity that was correlated with sleep health in our cohort.

The analysis revealed distinct correlation patterns between the symptom scales and the two hepatic indices. While the total scores of CSHQ and GSRS did not correlate with either index, the subscale analysis provided more nuanced insights. The HSI, primarily reflecting the degree of fat accumulation, showed limited and weak correlations with only a few specific subscales

(sleep-onset delay, sleep duration, and reflux). In contrast, the NFS, which estimates the risk of advanced fibrosis and encapsulates a broader profile of metabolic dysfunction (including age, BMI, and diabetes), demonstrated significant correlations with a wider array of both sleep disturbances (bedtime resistance, sleep-onset delay, sleep duration, sleep anxiety, night wakings, and parasomnias) and gastrointestinal symptoms (reflux and diarrhea). The strength of these correlations was notably higher for sleep anxiety and sleep duration. This divergence suggests that the extra-hepatic manifestations in sleep and gastrointestinal domains may be more closely linked to the underlying metabolic burden and disease progression risk (as approximated by fibrosis risk scores) than to the presence of hepatic steatosis. This interpretation aligns with the existing literature. A meta-analysis reported that obstructive sleep apnea is associated with progressive hepatic fibrosis (30), and a recent study showed a link between sleep duration and hepatic steatosis (31). Zong et al. (32) found that later bedtimes were associated with the degree of liver fibrosis, suggesting that circadian disruption may adversely affect metabolic hormones and promote fibrosis. Furthermore, our finding that NFS correlated with sleep disturbances, as well as with gastrointestinal symptoms like reflux and diarrhea, could indicate that advancing disease severity (fibrosis risk) may exacerbate extra-hepatic manifestations by amplifying systemic inflammation.

Our findings align with the understanding of pediatric MASLD as a manifestation of a broader metabolic dysfunction. Although the diagnosis of MASLD itself was not an independent sleep risk factor after metabolic adjustment, the cluster of conditions that include obesity, insulin resistance, gastrointestinal symptoms, and sleep disturbances frequently co-exist. The strong independent associations of gastrointestinal symptoms and insulin resistance with sleep problems highlight potential direct mechanistic pathways beyond hepatic steatosis. Furthermore, the fact that the severity of liver disease, as reflected by the NFS, showed broader and stronger correlations with both sleep and gastrointestinal symptoms, suggests that the systemic burden of the underlying metabolic disorder may be greater in those with a higher risk of disease progression. This pattern of associations reinforces the clinical recommendation that a child presenting with obesity and MASLD should be evaluated within a multidisciplinary framework that proactively screens for and manages sleep disturbances, gastrointestinal symptoms, and insulin resistance, addressing the root metabolic and socioeconomic contributors to improve overall health and quality of life.

Study Limitations

The strengths of our study include: (i) well-characterized patient and control groups, (ii) good socio-demographic matching

between groups, (iii) the use of valid and reliable scales (CSHQ, GSRS), and (iv) comprehensive statistical analyses examining relationships through multivariate analyses. However, the limitations of the study can be listed as follows. First, the cross-sectional design may limit our ability to establish direct causal relationships between variables. Second, the CSHQ and GSRS scores are based on parent- or self-reports, which, due to participants' subjective perceptions, could introduce bias. Moreover, the simultaneous use of these subjective instruments assessing the same recall period (past week) raises the possibility of common method bias, which could inflate the observed associations between gastrointestinal symptoms and sleep disturbances. Third, we did not collect data on hypertension, a component of metabolic syndrome that could influence both sleep architecture and gastrointestinal motility. Fourth, pubertal stage was not assessed using standardized methods (e.g., Tanner staging). Although age was included as a covariate in all analyses and was similar between groups, the potential confounding effect of pubertal hormonal changes on our outcomes cannot be ruled out. Fifth, the diagnosis and grading of hepatic steatosis relied on ultrasonography, which is operator-dependent. Although all scans were performed by a single experienced radiologist to minimize inter-observer variability, we did not formally assess intra-observer reliability, which is a methodological limitation. Sixth, the absence of an obese control group without MASLD limits our ability to determine whether the observed associations with sleep and gastrointestinal symptoms are specific to MASLD pathophysiology or are related to obesity more broadly. Future studies including this control group would help clarify the unique contribution of hepatic steatosis and metabolic dysfunction.

Clinical Implications and Future Directions

Our findings carry implications for the management of children with MASLD. First, they promote a shift from a purely hepatocentric view to a holistic, multi-system assessment. We suggest that routine clinical evaluation of children with MASLD should incorporate screening for sleep disturbances and gastrointestinal symptoms. Particular attention should be paid to patients from lower socioeconomic backgrounds and those with pronounced insulin resistance or gastrointestinal symptoms, as these factors were independently associated with sleep problems. Second, management strategies should be equally comprehensive. Addressing sleep hygiene, treating specific gastrointestinal symptoms, notably reflux and diarrhea, and intensifying efforts to improve insulin sensitivity through lifestyle interventions could be associated with improvements in both quality of life and metabolic health outcomes in these children. A proposed screening algorithm to identify children with MASLD at high risk for sleep disturbances, based on our key findings, is presented in Figure 2.

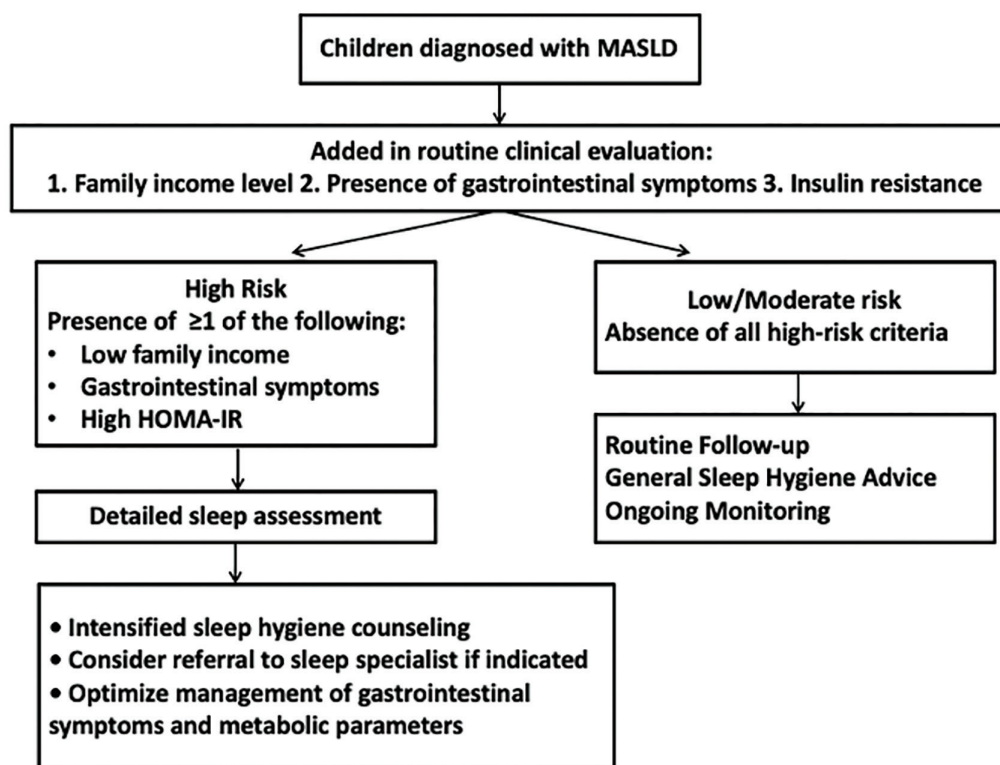


Figure 2. Proposed clinical screening algorithm for identifying children with metabolic dysfunction-associated steatotic liver disease who are at high risk for sleep disturbances

Conclusion

This study demonstrated a high prevalence of sleep disturbances and gastrointestinal symptoms in children with MASLD. After adjusting for key metabolic confounders, sleep disturbances were independently associated with low family income, gastrointestinal symptom severity, and insulin resistance. The risk of liver fibrosis, as indicated by the NFS, was further associated with a broader range of sleep and gastrointestinal symptoms. These cross-sectional findings indicate that in children with MASLD, sleep problems show a stronger association with underlying metabolic dysfunction, especially insulin resistance, and concurrent gastrointestinal distress than with MASLD. Therefore, the clinical management of children with MASLD should adopt a holistic approach that includes routine screening for sleep disturbances and gastrointestinal symptoms, with particular attention to those from lower socioeconomic backgrounds and/or with evidence of insulin resistance. Future longitudinal studies are needed to examine the impact of managing sleep, gastrointestinal symptoms, and insulin resistance on the progression of MASLD and to investigate underlying mechanisms, that may include cytokine profiles, gut microbiota, and autonomic nervous system function.

Ethics

Ethics Committee Approval: The study protocol was approved by the Antalya Training and Research Hospital Scientific Ethics Committee for Medical Research (date: 05.12.2024, approval no.: 19/21) prior to commencement.

Informed Consent: Informed consent in this study was taken from all participants.

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Footnotes

Authorship Contributions

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