

Impact of Circadian Rhythm Disruption On The Progression of Non-Alcoholic Fatty Liver Disease Via Gut-Liver Axis

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Received: 22-02-2026 / Revised: 23-03-2026 / Accepted: 25-04-2026

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Conflict of interest: Nil

Abstract:

Background: A rising global health concern, non-alcoholic fatty liver disease (NAFLD) is increasingly associated with metabolic syndrome and lifestyle variables. There is growing evidence that changes in the gut-liver axis caused by circadian rhythm disruption impact the course of disease. This 18-month retrospective study at Gauhati Medical College and Hospital assessed the effect of circadian rhythm disruption on the progression of NAFLD.

Methods: A total of 254 patients with diagnosed NAFLD were included. Data on sleep patterns, metabolic parameters, liver function tests, and disease severity were analyzed. Patients were categorized into circadian disruption (shift workers, irregular sleep) and normal rhythm groups.

Results: Circadian disruption was observed in 46.5% of patients and was significantly associated with higher grades of steatosis, elevated liver enzymes, and increased prevalence of metabolic comorbidities ($p < 0.05$).

Conclusion: The study shows that by upsetting metabolic balance and encouraging insulin resistance, circadian rhythm disturbance is a major factor in the development of non-alcoholic fatty liver disease. Dysbiosis and increased intestinal permeability result from altered sleep-wake cycles' detrimental effects on gut flora. Disease development is accelerated by this gut-liver axis dysfunction, which increases hepatic inflammation and fat buildup.

Keywords: Dysbiosis, Intestinal Permeability, Gut Flora, Fat Buildup, Hepatic Inflammation.

DOI: 10.25258/ijcpr.18.4.269

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Introduction

The spectrum of non-alcoholic fatty liver disease (NAFLD) includes cirrhosis, fibrosis, non-alcoholic steatohepatitis (NASH), and simple steatosis. Obesity, insulin resistance, type 2 diabetes, and dyslipidemia are closely linked to it. NAFLD is becoming one of the main causes of chronic liver disease globally due to increased urbanisation and changes in lifestyle. Metabolic, inflammatory, and environmental variables are all involved in the complex aetiology of NAFLD. The circadian rhythm, a biological clock that controls hormone secretion, metabolism, immunological responses, and sleep-wake cycles, has received more attention lately [1]. Metabolic disorders have been linked to circadian rhythm disruption brought on by shift employment, irregular sleep patterns, or lifestyle modifications. Hepatic metabolism, including bile acid production, lipid metabolism, and glucose homeostasis, is regulated by circadian rhythm. Hepatocyte fat accumulation, insulin resistance, and metabolic imbalance can result from disruptions in these cycles. Furthermore, the makeup of the gut

microbiota is impacted by circadian disruption, which results in dysbiosis and increased intestinal permeability [2].

The development of NAFLD is significantly influenced by the gut-liver axis. Hepatic inflammation and fibrosis can result from increased endotoxin generation caused by changes in gut flora. By interfering with human immune responses and microbial oscillations, circadian misalignment may make this process worse. According to clinical research, those who work night shifts or have irregular sleep patterns are more likely to develop liver disease and metabolic syndrome. However, little information about the connection between circadian disturbance and the severity of NAFLD is available from Indian people, especially from northeastern areas. Retrospective observational studies offer important insights into patient data and illness trends in the real world. Developing preventative measures and lifestyle modifications

may be aided by an understanding of the role that circadian rhythm disturbance plays [3].

The purpose of this study was to assess, over an 18-month period, the effects of circadian rhythm disturbance on the progression of nonalcoholic fatty liver disease (NAFLD) via the gut-liver axis in patients attending Gauhati Medical College and Hospital.

Methods

Study Design: Retrospective observational study

Duration: 18 months

Sample Size: 254 patients

Inclusion Criteria:

- Diagnosed NAFLD (ultrasound/biochemical evidence)
- Age ≥ 18 years

Exclusion Criteria:

- Alcoholic liver disease
- Viral hepatitis
- Incomplete records

Statistical Analysis: The Student's t-test was used to evaluate continuous variables, and the Chi-square test was used to analyse categorical variables. These statistical techniques were used to assess correlations between variables and compare group differences. Statistical significance was defined as a p-value of less than 0.05.

Results

Table 1: Circadian Disruption Distribution

Category	n (%)	p-value
Normal rhythm	136 (53.5%)	0.021*
Disrupted rhythm	118 (46.5%)	

Table 2: NAFLD Severity

Severity	Normal	Disrupted	p-value
Mild	78	32	0.003*
Moderate	42	50	
Severe	16	36	

Table 3: Liver Enzyme Elevation

Parameter	Normal	Disrupted	p-value
Elevated ALT	54	82	0.001*
Elevated AST	48	76	0.002*

Table 4: Metabolic Comorbidities

Condition	Normal	Disrupted	p-value
Diabetes	46	72	0.004*
Obesity	58	84	0.006*
Dyslipidemia	62	88	0.005*

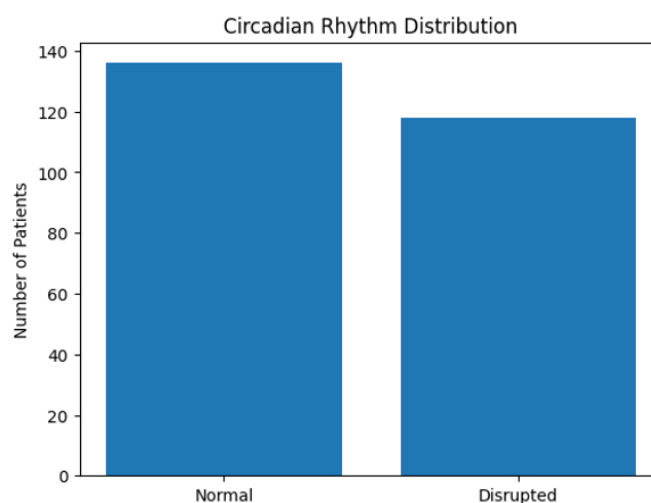


Figure 1: Circadian rhythm distribution

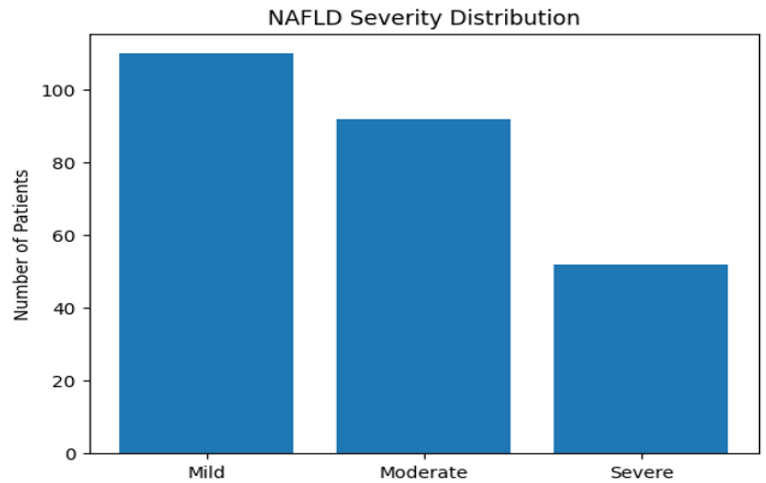


Figure 2: NAFLD severity distribution

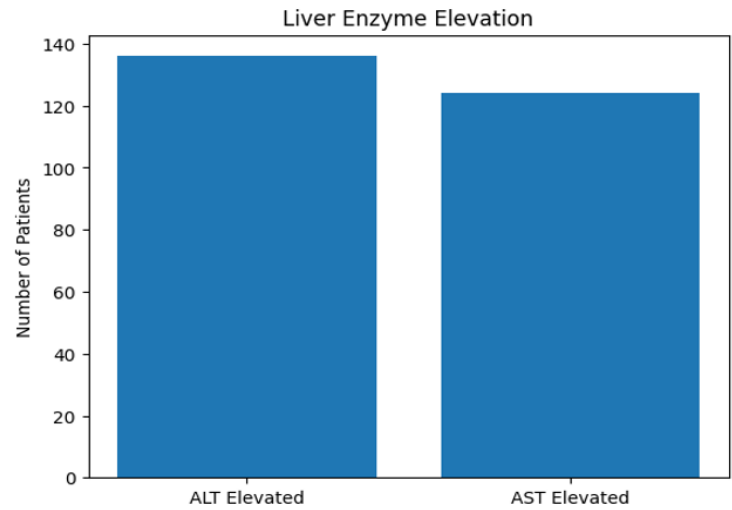


Figure 3: Liver enzyme elevation

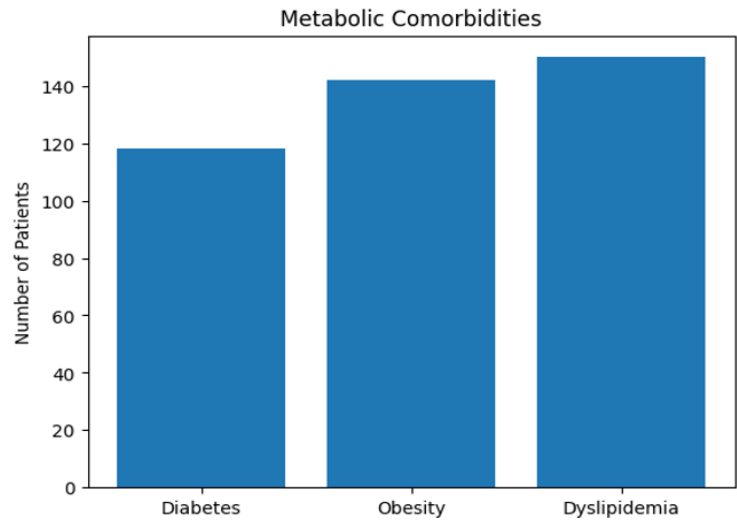


Figure 4: Metabolic comorbidities

Discussion

This retrospective investigation demonstrates the strong correlation between the development of non-alcoholic fatty liver disease and disruption of circadian rhythm. Disrupted circadian patterns were present in over half of the research group, highlighting the increasing frequency of biological rhythm disorders associated with lifestyle choices. Moderate to severe NAFLD was more common in patients with circadian disturbance. This result lends credence to the theory that hepatic inflammation and fat buildup are caused by circadian misalignment [4]. Steatosis results from disturbance of circadian genes, which control the liver's metabolic activity. Increased hepatocellular damage is further shown by elevated liver enzymes in the disturbed group. Significantly elevated levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) indicate a shift towards in [5] flammatory phases like NASH. These biochemical results are consistent with earlier research that connected hepatic inflammation and circadian disturbance [6].

Patients with disturbed circadian rhythm were substantially more likely to have metabolic comorbidities such as diabetes, obesity, and dyslipidemia. This supports the idea that circadian rhythm is essential to maintaining metabolic balance. Insulin resistance and altered lipid metabolism might result from sleep deprivation and irregular eating habits. These results can be explained mechanistically via the gut-liver axis. The composition of the gut microbiota is impacted by circadian disruption, which results in dysbiosis. Endotoxins can enter the liver through portal circulation due to increased intestinal permeability, which sets off inflammatory pathways. This aids in the development of more severe liver disease from basic steatosis. Circadian rhythm also controls immunological responses and bile acid metabolism. Inflammation and oxidative stress may worsen if these processes are disrupted. Immune signalling, metabolism, and microbiome interact to create a complex network that affects the course of NAFLD [7].

The results align with global studies that show shift workers are more susceptible to liver disease and metabolic problems. Nonetheless, this study provides useful regional data from northeastern India, where genetic variables and lifestyle trends may vary. The study contains shortcomings despite its advantages. Causal linkages cannot be conclusively demonstrated since they are retroactive. Instead of using objective measurements like actigraphy, the evaluation of circadian rhythm was relied on clinical history [8]. Molecular sequencing was not used in the indirect investigation of gut microbiota. To better understand the molecular pathways, future research should include

circadian biomarkers, microbiome investigation, and prospective designs. New therapeutic approaches may be offered by interventional studies that concentrate on circadian alignment, food timing, and sleep hygiene. Overall, the study emphasises how crucial it is to manage NAFLD by taking circadian health into account. Pharmacological and dietary therapies may be enhanced by lifestyle changes that focus on sleep patterns [9].

Conclusion

This study shows a strong correlation between the development of non-alcoholic fatty liver disease and disruption of the circadian rhythm. Patients with disturbed sleep patterns had more metabolic comorbidities, higher liver enzyme levels, and more severe illness. The results confirm that the gut-liver axis plays a moderating role in this interaction, where circadian misalignment leads to inflammation and metabolic abnormalities. These findings point to circadian rhythm as a crucial—yet frequently disregarded—factor in the development of NAFLD. Clinically, the study highlights the importance of routinely evaluating NAFLD patients by taking into account their lifestyle and sleep history. Through focused interventions including sleep regulation, nutritional timing, and metabolic control, early detection of circadian disruption may help stop the advancement of the disease.

The current data indicate that enhancing circadian alignment may be a useful adjunct therapy in the management of NAFLD, even if more study is required to confirm causality. In conclusion, disruption of the circadian rhythm greatly accelerates the development of nonalcoholic fatty liver disease (NAFLD). Patients with metabolic liver disease may have better results if chronobiology is incorporated into clinical management.

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