Advances in Bioresearch
Adv. Biores., Vol 16 (3) May 2025: 289-299

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.16.3.289299

Advances in Bioresearch

ORIGINAL ARTICLE

An observational study on treatment strategies in nonalcoholic fatty liver disease and Nonalcoholic steatohepatitis

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ABSTRACT
NASH is a significant contributor to cirrhosis and is accompanied by various comorbidities. Understanding the prevalence, associated conditions, and treatment strategies for NASH is crucial for effective management. This study aims to evaluate these aspects in a cohort of patients diagnosed with NASH. We conducted a multicenter observational study involving 130 patients with NAFLD or NASH. Data were collected on demographics, BMI, comorbidities, liver function, and pharmacological treatments through patient interviews, medical records, and laboratory results. Statistical methods were used to analyze the collected data. The study cohort included 59 males (45.38%) and 71 females (54.61%). Among the patients, 56.92% were classified as overweight, and 43.07% as obese. Comorbid conditions were present in 81.53% of patients, with hypertension (27.69%), diabetes mellitus (22.30%), hyperlipidemia (33.07%), and hypertriglyceridemia (34.61%) being the most common. Fibroscan assessments revealed that 76.15% of patients had moderate fibrosis (F2). The primary pharmacological treatments were atorvastatin (68.46%), ursodeoxycholic acid (52.30%), vitamin E (44.61%), and fenofibrate (43.84%). Metformin and pioglitazone were frequently used for diabetes management, and saroglitazar was prescribed in 10.76% of cases for liver damage, especially in those with diabetic dyslipidemia. This study highlights the significant burden of comorbidities in NASH patients and the careful use of hypolipidemic agents, antioxidants, and antidiabetic medications. Effective management of NAFLD and NASH requires a comprehensive approach that includes lifestyle modifications and pharmacotherapy to prevent disease progression.
Keywords: *Non-alcoholic fatty liver disease, Non-alcoholic steatohepatitis, Treatment strategies, Metabolic dysregulation, Comorbidities, Liver fibrosis.*

Received 12.03.2025 Revised 06.04.2025 Accepted 11.05.2025

How to cite this article:
Sattwik J Paul, Aniket N Lalaji, Anas Jamsa, Gunosindhu Chakraborthy. S P Srinivas Nayak. An observational study on treatment strategies in nonalcoholic fatty liver disease and nonalcoholic steatohepatitisAdv. Biores., Vol 16 (3) May 2025: 289-299.

INTRODUCTION

Hepatic steatosis is a sign of NASH, increasingly recognized as a primary factor inducing long-term hepatic disorder worldwide when there is no significant consumption of alcohol[1].Progression of NAFLD, liver damage secondary to lipotoxicity, oxidative burden as well as ER burden increased markedly [1]. Prevalence of steatosis varies from ≥5% detectable hepatocytes in NAFLD [1], to the entire spectrum of hepatic damage up into obese and DM II patients, subjects with metabolic threats. Schaffner introduced the term " NAFLD" in 1986 [2]. The development of NASH as well as insulin resistance in DM II patients amplifies their risk further, as indicated by excessive hepatic fat accumulation being a clinical hallmark of the disease [3]. NASH, a disease categorised as general fatty liver at the early stage of its development to cirrhosis and even hepatocellular cancer [4]. Prevent the disease with early intervention and preventive lifestyle changes to reduce risk factors [5]. Cellular characteristics indicate that NAFLD as well as NASH are both primary types of NAFLD [6]. Additionally, among obese children, the risk of NAFLD varies from 2% to 44% in Europe, while occurrences of DM II were typically 43% to 70% [7]. Indian subgroups had greater hepatic fat content and insulin resistance in comparison to other ethnicities [5]. Inconsistent diagnostic criteria have left the occurrence of NAFLD and NASH unreliable, despite improving global

awareness [8]. In accordance of a large-scale study, ninety-one percentage of overweight people with a BMI of over 30 kilograms per square of metre was affected with fatty liver when tested using ultrasonography [9]. Furthermore, there is ongoing research over the occurrences of NAFLD over the Indian subcontinent as well as the variations in its clinicopathology when compared with populations in the West [10]. A hike in NAFLD collision may be associated with the rising instances of diabetes, overweight, as well as insulin resistance in Indian subcontinent [10], and SGPT-SGOT ratio is a significant indicator for distinguishing NAFLD from ALD [11]. Obesity, type 2 diabetes, dyslipidemia, hypertriglyceridemia, cyclic weight loss, and hypertension are risk factors for NAFLD [12]. Since excess adipose substituents in the hepatic tissue triggers inflammation as well as fibrosis, preventing these disorders is essential for controlling NAFLD [13]. Reports indicate that many pathways, including as Wnt signaling and the impact of the p53 tumor suppression gene, are involved in the growth of NAFLD and NASH [14-16]. Based on recent research, pioglitazone and vitamin E are useful therapies for NAFLD [17]. But there are currently no authorized drugs for NAFLD, and most available therapies are used off-label [17]. Pharmacological therapies that target important pathways such hepatic fibrosis, inflammation, oxidative stress, and apoptosis have become more and more important for management of NAFLD and NASH currently [18]. These disorders are also significantly influenced by the gut-liver axis, which comprises inflammation, metabolic endotoxemia, gut microbiomes, and bile acids[18]. A number of pharmaceutical products, such as GLP-1 receptor agonists and insulin sensitizers like metformin, have demonstrated potential advantages in managing NASH. Metformin, frequently used in increasing insulin sensitivity and boosts the release of hepatic enzymes and insulin sensitivity, although its effect on liver histology is still very small [19]. The GLP-1 receptor agonists like liraglutide possess potential hepatic fat reduction ability and liver function improvement capability that looks promising in the treatment of NAFLD/NASH [20, 21]. Novel therapeutic avenues targeting FXR agonists, PPARα/δ dual and pan-agonist are also actively being investigated for their ability to regulate lipid metabolism as well as fibrosis in the liveropathies, further broadening the pharmacological options available [22, 23]. Imaging techniques and biochemical markers are used for the detection of presence (but not importantly absence) of NAFLD, as well as to differentiate between fatty liver alone vs. more severe NASH [24]. Novel therapeutic approaches have attempted to disrupt the pathophysiology of the disease with regard to lipid peroxidation and metabolic syndrome pathways [25]. Pharmacological therapies that target important pathways such hepatic fibrosis, inflammation, oxidative stress, and apoptosis have become more and more important for management of NASH recently [18]. These disorders are also significantly influenced by the gut-liver axis, which comprises inflammation, metabolic endotoxemia, gut microbiomes, and bile acids[18].NAFLD and NASH might respond better with a variety of drugs, including GLP-1 receptor agonists and insulin sensitizers like metformin. Metformin, for example, is often used to increase insulin sensitivity and boosts the release of hepatic enzymes and insulin sensitivity, although its effect on liver histology is still very small [19]. GLP-1 receptor agonists like liraglutide are an appealing option of NAFLD/NASH management because they have shown promise in lowering the amount of fat in the liver and enhancing liver function [20, 21]. Further altering the pharmacological landscape for these liver illnesses are novel treatment methods utilizing FXR agonists and PPAR agonists that are being investigated for their ability to alter lipid metabolism and decrease fibrosis [22, 23].

MATERIAL AND METHODS

Study Design and Setting

This was a multicenter, observational study conducted at two medical institutions: Parul Sevashram Hospital, Waghodia, and the International Gastro Institute, Vadodara, Gujarat. The study aimed to evaluate the prevalence of comorbidities and pharmacological treatment strategies in patients diagnosed with non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH). Data were collected retrospectively from patients' medical records over a six-month period.

Study Population

A total of 130 patients, both male and female, with confirmed diagnoses of NAFLD or NASH, were included in the study. Patients were selected based on the following criteria:

Inclusion Criteria

- Patients of all ages and both genders, with a confirmed diagnosis or suspected diagnosis of NAFLD or NASH, were eligible for inclusion in the study.
- Patients with any form of hepatic disease.

Exclusion Criteria

- Patients unwilling to participate or unable to provide informed consent.
- Pregnant women diagnosed with NAFLD or NASH.

Data Collection

Data were obtained using a structured patient data collection form, which included information on demographics (age, gender), body mass index (BMI), medical history, comorbid conditions, laboratory investigations, and treatment details. Data were gathered from the patients' outpatient department (OPD) records, hospital medical files, and laboratory reports.

Assessment of Comorbidities

Comorbid conditions such as hypertension, diabetes mellitus, hyperlipidemia, hypertriglyceridemia, hypothyroidism, and hyperthyroidism were documented. Additionally, the presence of diabetic dyslipidemia and other metabolic disorders was noted.

Liver Function and Fibrosis Assessment

Liver function was evaluated using laboratory markers, including aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels. Fibrosis was assessed using non-invasive methods, primarily Fibroscan and ultrasound, to categorize patients into mild (F1), moderate (F2), and severe fibrosis (F3) groups. These scores were further corroborated by ultrasound findings indicating the severity of fatty infiltration in the liver.

Pharmacological Treatment

The study also evaluated the pharmacological treatment strategies employed in the management of NAFLD and NASH. The medications used were categorized as hypolipidemic agents, antioxidants, and antidiabetic medications. Commonly prescribed medications included atorvastatin, ursodeoxycholic acid, vitamin E, fenofibrate, metformin, pioglitazone, and saroglitazar.

Data Analysis

Data were entered into Microsoft Excel and statistically analyzed. Descriptive statistics, including counts and percentages, were used to summarize categorical variables. Mean values and standard deviations were calculated for continuous variables. Graphical displays were used to present the data for better visualization, and figures and tables were created to summarize the results.

Ethical Considerations

Ethical approval for the study was obtained from the Institutional Ethics Committee of Parul Sevashram Hospital, Waghodia, Vadodara, Gujarat (PUIECHR/PIMSR/00/081734/6501). The study was conducted following the ethical guidelines for biomedical research involving human subjects, and informed consent was obtained from all patients before data collection.

RESULTS

Our study analysed data from 130 patients, comprising 59 males and 71 females. We evaluated the results by calculating the mean values and assessing them according to their BMI, comorbidities, lab reports, and treatments. The detailed analysis is provided below,

Table.1: Drug Utilization Overview in overall patients

Drugs	Percentage	No. of patients (N=130)
METFORMIN	22.30%	29
UDIHEP	52.30%	68
VIT-E	44.61%	58
SAROGLITAZAR	10.76%	14
ATORVASTATIN	68.46%	89
FENOFIBRATE	43.84%	57
PIOGLITAZONE	17.69%	23
Omega-3-fatty acid	11.53%	15
Multi Vitamin	33.07%	43

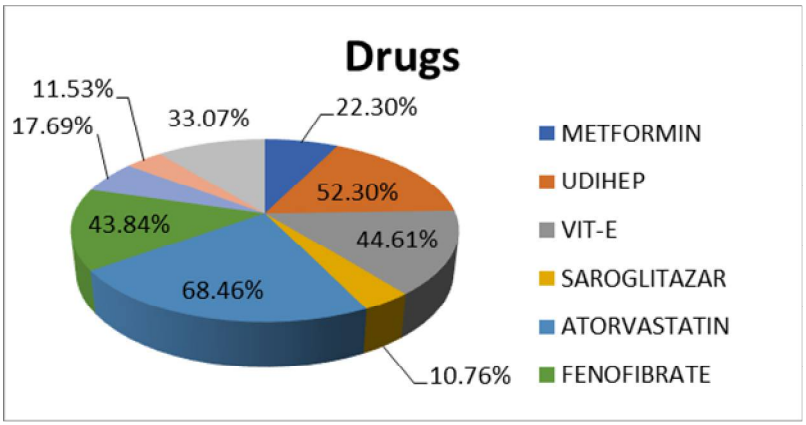

Figure.1 : Drug Utilization Overview(Schematic representation of the study design outlining the treatment strategies for nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH).)

Table.2: OVERALL RESULTS

PARAMETERS	PERCENTAGE	NO. OF PATIENTS	MEAN VALUE
Gender Wise Distribution			
Male	45.38%	59	$\bar{X}$ =65
Female	54.61%	71	
Total	**100%**	**N=130**	
BMI (Over Weight)			
Male	44.59%	33	$\bar{X}$ =37
Female	55.40%	41	
Total	**100%**	**N=74**	
BMI (Obese)			
Male	46.42%	26	$\bar{X}$ =28
Female	53.57%	30	
Total	**100%**	**N=56**	
According to Disease			
Without Comorbidities	18.46%	24	$\bar{X}$ =65
With Comorbidities	81.53%	106	
Total	**100%**	**N=130**	
HTN			
Male	47.22%	17	$\bar{X}$ =18
Female	52.77%	19	
Total	**100%**	**N=36**	
DM			
Male	58.62%	17	$\bar{X}$ =14.5
Female	41.37%	12	
Total	**100%**	**N=29**	
HYPERLIPIDEMIA			
Male	51.16%	22	$\bar{X}$ =21.5
Female	48.83%	21	
Total	**100%**	**N=43**	
Hypertriglyceridemia			
Male	42.22%	19	$\bar{X}$ =22.5
Female	57.77%	26	
Total	**100%**	**N=45**	
Hypothyrodism			
Male	31.81%	7	$\bar{X}$ =11
Female	68.18%	15	
Total	**100%**	**N=22**	
Hyperthyrodism			
Male	45%	9	$\bar{X}$ =10
Female	55%	11	
Total	**100%**	**N=20**	
Diabeticdislipidemia			

Male	47.82%	11	$\bar{X}$ =11.5
Female	52.17%	12	
Total	**100%**	**N=23**	
Fibroscan score			
F1	10.76%	14	$\bar{X}$ =43.3
F2	76.15%	99	
F3	13.07%	17	
Total	**100%**	**N=130**	
Ultrasound Report			
Mild	10.76%	14	$\bar{X}$ =43.3
Moderate	76.15%	99	
Severe	13.07%	17	
Total	**100%**	**N=130**	
Laboratory Reports			
Triglycerides			
100-200	13.07%	17	$\bar{X}$ =26
200-300	50%	65	
300-400	20%	26	
400-500	7.69%	10	
>500	9.23%	12	
Total	**100%**	**N=130**	
Ferritin			
<300	51.53%	67	$\bar{X}$ =65
>300	48.46%	63	
Total	**100%**	**N=130**	
AST			
<50	11.53%	15	$\bar{X}$ =32.5
50-60	37.69%	49	
60-70	40.76%	53	
>70	10%	13	
Total	**100%**	**N=130**	
ALT			
50-60	3.07%	4	$\bar{X}$ =26
60-70	25.38%	33	
70-80	36.92%	48	
80-90	24.61%	32	
>90	10%	13	
Total	**100%**	**N=130**	

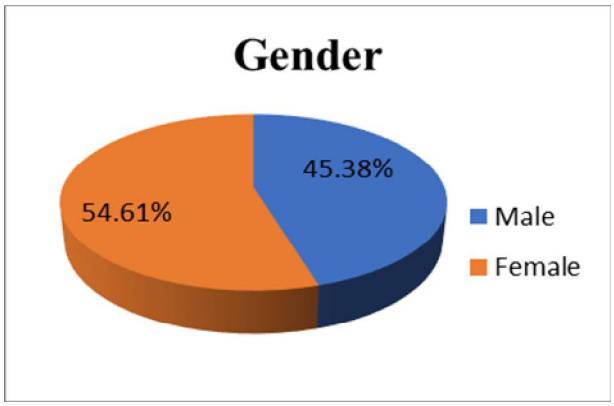

Figure.2 : Gender wise Distribution (The gender distribution of the study population, indicating that 54.61% were female and 45.38% were male.)

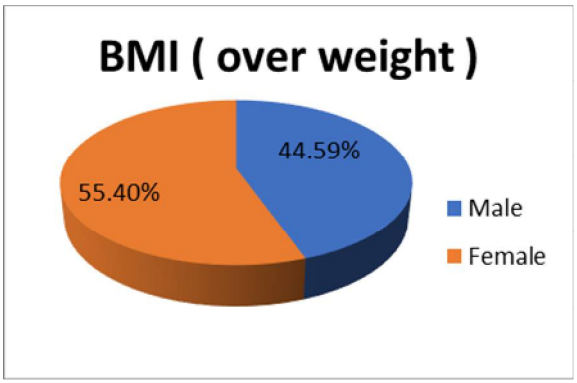

Figure.3 : BMI (Overweight) wise Distribution(The distribution of participants classified as overweight, showing that 55.40% of the overweight participants were female, while 44.59% were male.)

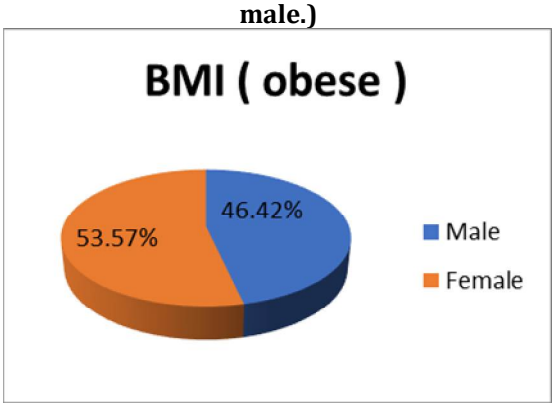

Figure.4 : BMI (Obese) wise Distribution(The gender distribution among participants classified as obese, with 53.57% being female and 46.42% male.) **S**

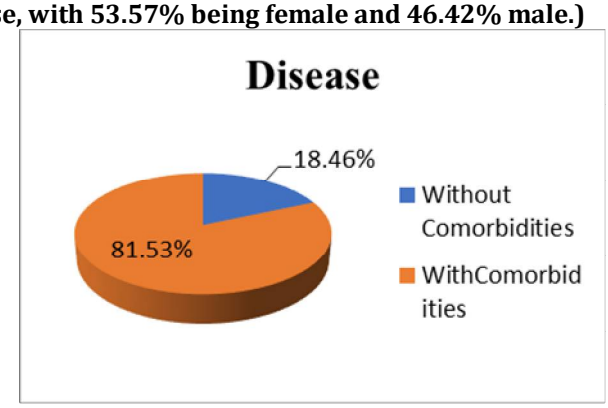

Figure.5 : Disease comorbidities wise Distribution (The prevalence of disease comorbidities in the study population, with 81.53% of participants having comorbidities and 18.46% without comorbidities.)

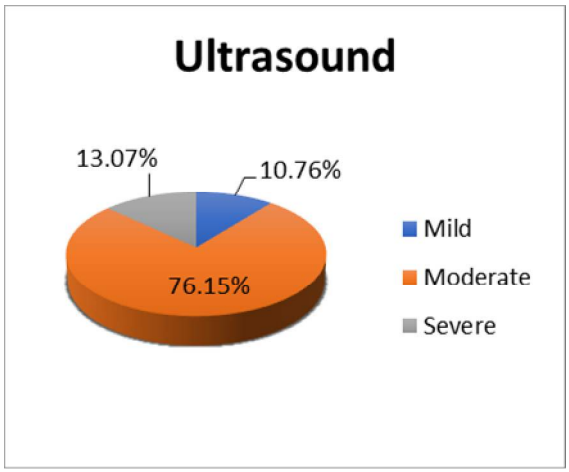

Figure.6 : Ultrasound wise Distribution (Ultrasound findings showing the distribution of disease severity, with 76.15% of patients presenting severe findings.)

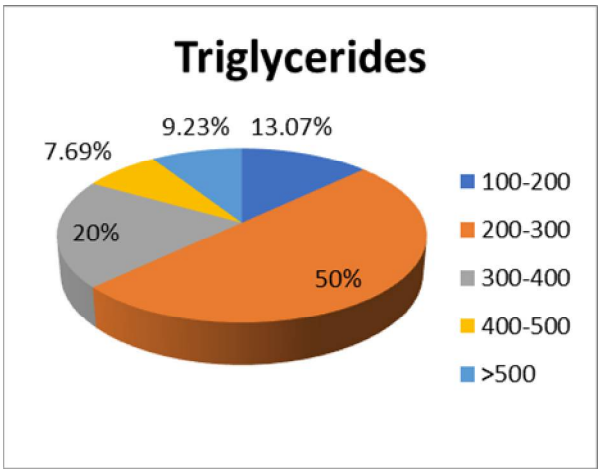

Figure.7 : Triglycerides wise Distribution (The distribution of triglyceride levels, with the largest group (50%) having triglyceride levels between 200 and 300 mg/dL.)

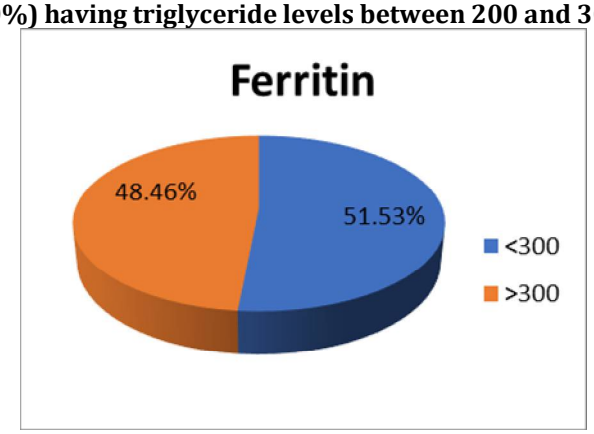

Figure.8: Ferritin wise Distribution (The distribution of ferritin levels, with 51.53% of participants having levels below 300 ng/mL and 48.46% with levels above 300 ng/mL.)

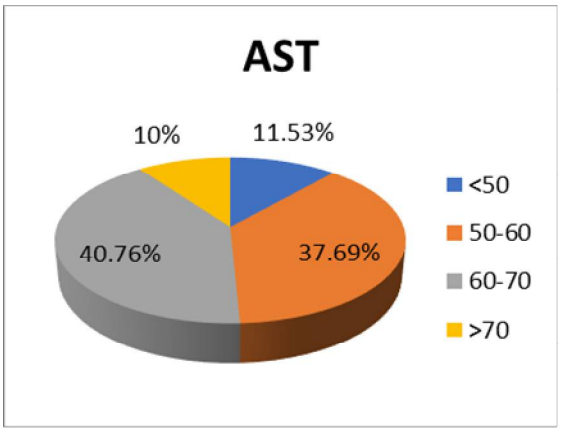

Figure.9: AST wise Distribution (The distribution of AST levels, showing that 40.76% of participants had AST levels between 50 and 60 U/L.)

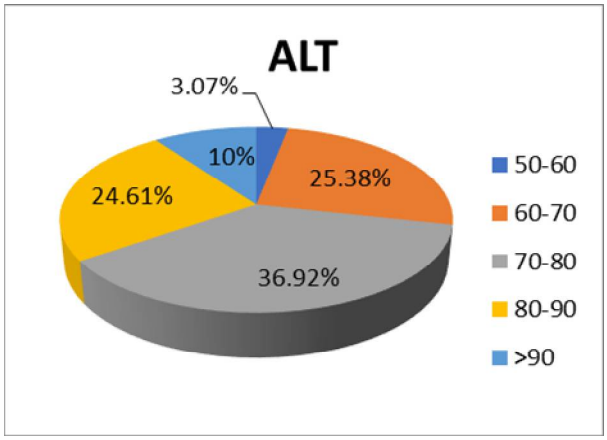

Figure.10: ALT wise Distribution (The distribution of ALT levels among participants, with 36.92% having ALT levels between 70 and 80 U/L.)

Demographic and Clinical Characteristics

The study comprised 130 patients, of whom 59 (45.38%) were male and 71 (54.61%) were female. The study population was 65 years old on average (± standard deviation). Of the patients, 56.92% were categorized as overweight and 43.07% as obese based on their body mass index (BMI). Of the male patients, 46.42% were fat and 44.59% were overweight. Likewise, 53.57% of female patients were fat and 55.40% were overweight.

Comorbidities

The majority of patients (81.53%) had at least one comorbidity. Hypertension was present in 36 patients (27.69%), with 47.22% of the male population and 52.77% of the female population affected. Diabetes mellitus was observed in 29 patients (22.30%), of whom 58.62% were males and 41.37% were females. Hyperlipidemia was diagnosed in 43 patients (33.07%), with a slightly higher prevalence in males (51.16%) than females (48.83%). Hypertriglyceridemia was present in 45 patients (34.61%), with a higher prevalence in females (57.77%) than in males (42.22%). Hypothyroidism was identified in 22 patients (16.92%), and hyperthyroidism in 20 patients (15.38%). Additionally, diabetic dyslipidemia was noted in 23 patients (17.69%).

Liver Fibrosis and Ultrasound Findings

Fibroscan scores were used to assess liver fibrosis severity. The majority of patients (76.15%) had moderate fibrosis (F2), while 10.76% had mild fibrosis (F1) and 13.07% had severe fibrosis (F3). Ultrasound findings corroborated these results, showing mild fatty infiltration in 10.76% of patients, moderate fatty infiltration in 76.15%, and severe fatty infiltration in 13.07%.

Laboratory Investigations

Triglyceride levels varied among patients, with 50% having levels between 200-300 mg/dL, 13.07% between 100-200 mg/dL, and 20% between 300-400 mg/dL. A smaller percentage of patients had triglyceride levels in the ranges of 400-500 mg/dL (7.69%) and >500 mg/dL (9.23%).

Ferritin levels were <300 ng/mL in 51.53% of the patients and >300 ng/mL in 48.46%, indicating potential hepatic injury in the latter group. Aspartate aminotransferase (AST) levels were elevated in 40.76% of patients, with levels ranging from 60-70 U/L. Alanine aminotransferase (ALT) levels were also elevated in 36.92% of patients, with levels between 70-80 U/L.

Pharmacological Treatments

Atorvastatin was the most commonly prescribed medication, used in 68.46% of patients (n=89). Ursodeoxycholic acid was prescribed to 52.30% (n=68), while 44.61% of patients (n=58) received vitamin E. Fenofibrate was prescribed in 43.84% of cases (n=57), primarily in patients with hyperlipidemia and hypertriglyceridemia. Saroglitazar, used for diabetic dyslipidemia, was prescribed in 10.76% of cases (n=14). Additionally, metformin was prescribed to 22.30% of patients (n=29), while pioglitazone was prescribed to 17.69% (n=23). Omega-3 fatty acids were administered to 11.53% of patients (n=15).

Summary of Findings

Overall, the study demonstrated that those with NAFLD and NASH had a significant frequency of concurrent conditions, such as hypertension, diabetes mellitus, and hypertriglyceridemia. The majority of patients exhibited moderate liver fibrosis and were treated with a combination of hypolipidemic agents, antioxidants, and antidiabetic medications. The results underscore the need for a comprehensive treatment approach, addressing both hepatic and metabolic risk factors, to effectively manage NAFLD and NASH.

DISSCUSSION

The findings of this observational study provide valuable insights into the prevalence of comorbidities and pharmacological treatment strategies in patients with NAFLD and NASH. Our study highlights the significant burden of metabolic comorbidities, including hypertension, DM-2, hyperlipidemia, and hypertriglyceridemia, in patients with NAFLD/NASH. These findings are consistent with previous research, which has established metabolic syndrome as a major risk factor for NAFLD and its progression to NASH. The high prevalence of moderate fibrosis (F2) observed in our cohort aligns with other studies that have found liver fibrosis to be a common feature in NAFLD patients with metabolic risk factors. Fibrosis progression is particularly concerning, as it increases the likelihood of cirrhosis and hepatocellular carcinoma. Our findings reinforce the need for early detection and intervention to prevent further liver damage. Pharmacological treatments in our study cohort primarily included atorvastatin, ursodeoxycholic acid, vitamin E, and fenofibrate. Atorvastatin was the most commonly prescribed medication, reflecting its widespread use in managing dyslipidemia and preventing cardiovascular complications in patients with metabolic disorders. Ursodeoxycholic acid and vitamin E, both used for their hepatoprotective properties, have been frequently studied in the context of NAFLD management. However, while vitamin E has shown efficacy in reducing liver fat and increasing hepatic histology in non-diabetic patients, its long-term safety remains uncertain. The use of saroglitazar in 10.76% of cases is notable, as this drug has recently emerged as a promising option for managing diabetic dyslipidemia and reducing hepatic fat accumulation. Saroglitazar's dual PPAR-α/γ agonist activity makes it an effective agent for treating both hypertriglyceridemia and hepatic steatosis, particularly in patients with DM-2. This highlights its potential role in the management of NAFLD/NASH in patients with comorbid diabetes and dyslipidemia. The findings from our study are consistent with global trends indicating a growing need for a comprehensive, multifactorial approach to the management of NAFLD and NASH. Weight loss, changes in nutrition, and daily physical activity persist to be the key components of therapy, and pharmacological treatment alone is inadequate. Patients with severe fibrosis or those who do not respond well to lifestyle changes alone should be considered for medications, consistent with clinical recommendations.

Clinical Implications

Our study emphasizes the importance of early intervention and the use of combination therapy to address both hepatic and metabolic risk factors in NAFLD/NASH patients. The significant use of statins, fibrates, and antioxidants in our cohort reflects current clinical practices aimed at mitigating cardiovascular risk and slowing disease progression. However, the lack of approved therapies for NAFLD/NASH remains a critical challenge in clinical practice, with most treatments being used off-label.

Limitations and Future Directions

This study has a number of limitations that should be noted. First, our findings might not be as applicable to larger populations due to the comparatively small sample size. Furthermore, selection bias may be

introduced by the study's retrospective design and reliance on medical data. Moreover, a thorough evaluation of the long-term safety and effectiveness of the used treatment approaches is not possible due to the lack of long-term follow-up data. For the purpose of assessing the long-term safety and efficacy of pharmaceutical therapies, future research should concentrate on longitudinal studies with bigger cohorts. To contribute to recommendations for treatment with more solid data, randomized controlled studies evaluating the combination of medication and lifestyle changes are also necessary. In addition, novel methods of treatment consisting of FXR and GLP-1 receptor agonists show promise and ought to be investigated further in the treatment of NAFLD and NASH (11).

CONCLUSION

In conclusion, this study underscores the complexity of managing NAFLD and NASH, particularly in patients with multiple metabolic comorbidities. While pharmacotherapy plays an important role in controlling metabolic risk factors and slowing disease progression, lifestyle interventions remain fundamental. Further research is needed to establish consider different perspective the optimal management of NAFLD and NASH, with approach on long-term outcomes and the development of new therapeutic agents.

ACKNOWLEDGEMENTS

We would like to express our sincere gratitude to the patients and staff at Parul Sevashram Hospital, Waghodia, and the International Gastro Institute, Vadodara, Gujarat, for their invaluable contributions to this study. We also extend our thanks to the Institutional Ethics Committee of Parul Sevashram Hospital for their support and guidance throughout the research process. Additionally, we acknowledge the efforts of all the healthcare professionals who assisted in the data collection and analysis. Special thanks to Parul University for providing the necessary resources for this study.

ABBRIVIATIONS:

NAFLD: Nonalcoholic fatty liver disease
NASH: Nonalcoholic Steatohepatitis
DM : Diabetes Mellitus
PCOS: Polycystic Ovary Syndrome
ALD: Alcoholic Liver Disease
AST: Alanine Aminotransferase
ALT: Aspartate Aminotransferase
SGPT: Serum Glutamic Pyruvic Transaminase
SGOT: Serum Glutamic Ocaloacetic Transaminase

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