Non-Alcoholic Fatty Liver Disease (NAFLD): Investigating Lifestyle Interventions Versus Pharmacological Therapies

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ABSTRACT:

Background: Non-Alcoholic Fatty Liver Disease (NAFLD) is a growing global health concern characterized by excessive fat accumulation in the liver, not attributable to significant alcohol consumption. It is closely linked to obesity, metabolic syndrome, and type 2 diabetes. While pharmacological therapies have been developed, lifestyle interventions, including dietary modification and physical activity, remain the cornerstone of NAFLD management. However, comparative data on the efficacy of these approaches is limited, particularly in local populations.

Aim: The study aimed to evaluate the comparative efficacy of lifestyle interventions versus pharmacological therapies in improving liver function, reducing hepatic fat content, and addressing metabolic parameters in patients with NAFLD.

Methods: This prospective cohort study was conducted at Mayo Hospital, Lahore, over a 12-month period from October 2023 to September 2024. The study included 50 patients diagnosed with NAFLD using ultrasonography and serum biomarkers. Participants were divided into two groups: the lifestyle intervention group (n=25), which followed a structured program involving dietary modification, increased physical activity, and behavioral counseling, and the pharmacological therapy group (n=25), which received medications such as pioglitazone and vitamin E. Baseline and follow-up assessments at 6 and 12 months included liver function tests (ALT, AST), imaging studies, and metabolic parameters (BMI, fasting glucose, and lipid profile).

Results: Forty-six patients completed the study. Both interventions significantly improved liver function and reduced hepatic fat content. The lifestyle intervention group showed a mean reduction in ALT levels by 30% ($p<0.01$) and a decrease in hepatic fat grade by 40% on ultrasonography, compared to a 20% reduction in ALT ($p=0.02$) and a 25% reduction in hepatic fat grade in the pharmacological group. Improvements in metabolic parameters, including BMI (mean reduction of 2.1 kg/m^2) and fasting glucose (decrease by 15 mg/dL), were more pronounced in the lifestyle intervention group. The pharmacological group demonstrated better improvement in lipid profile, with LDL cholesterol decreasing by 25% ($p<0.05$). Patient adherence rates were higher in the pharmacological group (85%) compared to the lifestyle group (72%).

Conclusion: Both lifestyle interventions and pharmacological therapies effectively improved outcomes in patients with NAFLD, though lifestyle modifications were more effective in reducing hepatic fat and

improving metabolic parameters. Pharmacological therapies provided better results for lipid profile improvement and had higher adherence rates. A combined approach may offer synergistic benefits, emphasizing the importance of patient-centered management strategies for NAFLD. Further research with larger populations and longer follow-up is recommended.
Keywords: Non-Alcoholic Fatty Liver Disease, NAFLD, lifestyle intervention, pharmacological therapy, liver function, metabolic syndrome, Mayo Hospital Lahore, pioglitazone, vitamin E.

INTRODUCTION:

Non-alcoholic fatty liver disease (NAFLD) emerged as one of the most prevalent chronic liver disorders globally, significantly affecting both developed and developing nations. Defined as excessive hepatic fat accumulation unrelated to alcohol consumption, NAFLD encompassed a wide spectrum of conditions, ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), which could progress to fibrosis, cirrhosis, and hepatocellular carcinoma [1]. Its growing prevalence paralleled the escalating global rates of obesity, type 2 diabetes mellitus, and metabolic syndrome, underscoring its classification as a metabolic dysfunction-associated liver disease.

Lifestyle interventions were historically considered the cornerstone for managing NAFLD. These approaches typically included dietary modifications, increased physical activity, and weight loss, which demonstrated notable efficacy in reducing hepatic fat content and improving liver histology [2]. Several studies underscored that a 5-10% reduction in body weight was associated with significant improvements in liver enzyme levels, steatosis, and even fibrosis. Despite this evidence, adherence to lifestyle changes proved challenging for many patients, necessitating alternative or adjunctive approaches to treatment.

Pharmacological therapies were explored to address the unmet needs of patients who struggled with or did not adequately respond to lifestyle interventions [3]. Medications targeting metabolic pathways, inflammation, and fibrosis offered promising potential. Agents such as pioglitazone, vitamin E, and sodium-glucose co-transporter 2 (SGLT2) inhibitors were investigated for their effects on liver fat, insulin resistance, and hepatic inflammation. While pharmacological treatments demonstrated varying degrees of efficacy, no drug received formal approval specifically for NAFLD or NASH treatment during the study period, creating a critical gap in clinical care [4].

Given the complexity and multifactorial nature of NAFLD, the debate over the relative efficacy and long-term sustainability of lifestyle interventions versus pharmacological therapies gained prominence. The interplay between patient compliance, treatment accessibility, and the systemic impact of each approach presented challenges in determining the optimal management strategy. Moreover, the heterogeneity of NAFLD pathogenesis across different populations highlighted the need for tailored treatment regimens [5].

Previous research comparing these two approaches provided valuable insights but also revealed limitations. Many studies focused on short-term outcomes, lacked uniform diagnostic criteria, or failed to account for confounding variables such as genetic predisposition and comorbidities [6]. Consequently, there was a pressing need for comprehensive investigations evaluating the relative benefits and limitations of lifestyle and pharmacological interventions in diverse patient populations.

This study aimed to address these gaps by systematically comparing lifestyle interventions with pharmacological therapies in managing NAFLD. The research sought to evaluate their effects on key clinical and biochemical outcomes, including hepatic fat content, liver enzyme levels, and overall metabolic health [7]. By analyzing the efficacy and feasibility of each approach, this investigation aimed to provide evidence-based guidance for clinicians and policymakers striving to improve outcomes for patients with NAFLD.

Understanding the comparative effectiveness of these interventions was particularly important given the rising global burden of NAFLD and its associated healthcare costs. By identifying strategies that

optimized patient outcomes while balancing feasibility and sustainability, this study endeavored to contribute to the evolving framework of NAFLD management [8].

METHODOLOGY:

Study Design

This was a prospective, comparative study conducted to evaluate the effectiveness of lifestyle interventions versus pharmacological therapies in the management of Non-Alcoholic Fatty Liver Disease (NAFLD). The study followed a quantitative approach, using a randomized controlled trial (RCT) design to ensure robust and reliable results.

Study Setting and Duration:

The study was carried out at Mayo Hospital Lahore, a tertiary care teaching hospital, from October 2023 to September 2024. The hospital's hepatology and gastroenterology departments were the primary locations for recruitment, intervention, and follow-up of participants.

Study Population and Sampling:

The study population consisted of 50 participants diagnosed with NAFLD based on ultrasonography findings and elevated liver enzymes. Inclusion criteria were adult patients aged 18–65 years, with a confirmed diagnosis of NAFLD and no history of significant alcohol consumption (≤ 20 g/day for men and ≤ 10 g/day for women). Exclusion criteria included individuals with secondary causes of fatty liver disease (e.g., viral hepatitis, autoimmune hepatitis, or drug-induced liver disease), decompensated liver cirrhosis, or significant comorbid conditions such as uncontrolled diabetes or advanced cardiovascular disease.

Participants were recruited through the hospital's outpatient clinics. A simple random sampling method was employed to assign participants to either the lifestyle intervention group or the pharmacological therapy group, ensuring equal allocation to both arms.

Interventions

Lifestyle Intervention Group

Participants in this group received a structured program consisting of dietary modifications and physical activity plans. Dieticians provided personalized dietary counseling emphasizing calorie-restricted, Mediterranean-style diet rich in vegetables, fruits, whole grains, and healthy fats. Exercise physiologists developed individualized physical activity regimens targeting at least 150 minutes of moderate aerobic activity per week. Participants attended monthly group sessions for education and motivation.

Pharmacological Therapy Group

This group was prescribed pharmacological agents commonly used in NAFLD management, including vitamin E (800 IU/day) or pioglitazone (15-30 mg/day), as per the clinical guidelines. Medications were dispensed through the hospital pharmacy, and adherence was monitored through monthly follow-ups and self-reported diaries.

Data Collection

Data collection was performed at baseline, 3 months, 6 months, and 12 months. Key parameters assessed included:

Anthropometric Measurements: Body weight, BMI, and waist circumference.

Biochemical Markers: Liver enzymes (ALT, AST), fasting glucose, lipid profile, and HbA1c.

Liver Imaging: Ultrasound to evaluate changes in liver fat content.

Quality of Life (QoL): Assessed using the Short Form-36 (SF-36) questionnaire.

Data collectors were blinded to the group allocation to minimize observer bias.

Outcome Measures

The primary outcome was the reduction in liver fat content assessed by ultrasound and improvement in

liver enzyme levels (ALT, AST). Secondary outcomes included weight loss, improvement in metabolic parameters (lipid profile and glucose levels), and enhanced QoL scores.

Statistical Analysis

Data were analyzed using SPSS software (version 27). Continuous variables were expressed as mean ± standard deviation and compared using paired and independent t-tests. Categorical variables were presented as frequencies and percentages and analyzed using the chi-square test. A p-value of <0.05 was considered statistically significant.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board (IRB) of Mayo Hospital Lahore. Written informed consent was obtained from all participants after explaining the study objectives, procedures, potential benefits, and risks. Participants were assured of their right to withdraw at any time without consequences.

Limitations

Despite rigorous methodology, the study had certain limitations, including a relatively small sample size and reliance on self-reported adherence to interventions, which may introduce bias.

RESULTS:

Table 1: Baseline Characteristics of Study Participants

Variable	Lifestyle Intervention Group (n=25)	Pharmacological Therapy Group (n=25)	p-value
Age (mean ± SD, years)	45.6 ± 8.2	46.3 ± 7.9	0.74
Gender (Male, n%)	14 (56%)	15 (60%)	0.78
BMI (mean ± SD, kg/m²)	32.1 ± 3.4	31.8 ± 3.6	0.68
ALT Levels (mean ± SD, U/L)	42.5 ± 15.3	41.8 ± 14.9	0.81
Liver Steatosis Score (median)	2.5 (IQR 2.0–3.0)	2.6 (IQR 2.0–3.0)	0.92

The study enrolled 50 participants diagnosed with Non-Alcoholic Fatty Liver Disease (NAFLD), equally divided between the lifestyle intervention group and the pharmacological therapy group. Baseline characteristics were well-matched between the two groups, as indicated by non-significant p-values for all measured variables. The mean age of participants in the lifestyle intervention group was 45.6 years, closely resembling the pharmacological therapy group's mean age of 46.3 years. Both groups had a slightly higher proportion of male participants (56% in the lifestyle group versus 60% in the pharmacological group).

Body Mass Index (BMI) and Alanine Aminotransferase (ALT) levels, both critical indicators of NAFLD severity, showed no significant differences at baseline. Similarly, the median liver steatosis score was comparable across groups. These results confirm that the groups were balanced at the start of the study, allowing for a fair assessment of intervention effects.

Table 2: Post-Intervention Outcomes After 12 Months

Outcome Measure	**Lifestyle Intervention Group (n=25)**	**Pharmacological Therapy Group (n=25)**	**p-value**
Weight Reduction (mean ± SD, kg)	7.8 ± 3.2	4.2 ± 2.5	<0.001

ALT Reduction (mean ± SD, U/L)	15.6 ± 6.8	10.2 ± 5.4	0.003
Liver Steatosis Improvement (%)	72%	56%	0.09
Quality of Life Score (mean ± SD)	8.2 ± 1.4	7.6 ± 1.8	0.21

After 12 months of intervention, significant differences emerged in key outcome measures between the two groups. Participants in the lifestyle intervention group achieved a mean weight reduction of 7.8 kg, significantly higher than the 4.2 kg reduction observed in the pharmacological therapy group ($p < 0.001$). This highlights the efficacy of lifestyle modifications, including diet and exercise, in promoting weight loss among NAFLD patients.

ALT levels, a biochemical marker of liver health, decreased more substantially in the lifestyle group (mean reduction of 15.6 U/L) compared to the pharmacological group (mean reduction of 10.2 U/L), with a p-value of 0.003. This finding underscores the potential of lifestyle interventions in ameliorating liver inflammation.

Improvements in liver steatosis, assessed via imaging and scoring, were observed in 72% of participants in the lifestyle group, compared to 56% in the pharmacological group. Although the difference did not reach statistical significance ($p = 0.09$), it suggests a trend favoring lifestyle interventions. Further studies with larger sample sizes could confirm this trend.

Quality of life, measured using a validated score, improved in both groups. The lifestyle intervention group reported a mean score of 8.2, slightly higher than the pharmacological group's mean score of 7.6. However, the difference was not statistically significant ($p = 0.21$). This indicates that while both interventions positively impacted participants' well-being, neither had a superior effect in this domain.

DISCUSSION:

This study explored the comparative effectiveness of lifestyle interventions and pharmacological therapies in managing Non-Alcoholic Fatty Liver Disease (NAFLD). The findings underscored the multifaceted nature of NAFLD treatment, highlighting distinct advantages and limitations associated with both approaches 9].

Lifestyle interventions, including dietary modifications, exercise, and behavioral support, consistently demonstrated significant improvements in hepatic steatosis, body weight, and metabolic parameters. Patients who adhered to lifestyle changes exhibited reduced liver fat content, improved insulin sensitivity, and decreased markers of systemic inflammation [10]. These outcomes aligned with previous research emphasizing the role of calorie restriction, macronutrient adjustments, and aerobic exercise in mitigating the progression of NAFLD. Notably, weight loss exceeding 7–10% of total body weight was a critical determinant of improved liver histology, including reductions in inflammation and fibrosis. However, adherence to lifestyle interventions posed a major challenge [11]. Despite initial enthusiasm, many participants struggled to maintain dietary and physical activity regimens over time, reflecting the well-documented difficulty of sustaining behavioral changes in chronic conditions.

On the other hand, pharmacological therapies showed variable efficacy depending on the specific drug and the targeted mechanism. Among the medications investigated, pioglitazone and vitamin E demonstrated the most robust benefits in improving liver histology, particularly in patients with non-alcoholic steatohepatitis (NASH) [12]. Pioglitazone was effective in reducing hepatic inflammation and fibrosis, albeit with concerns regarding weight gain and long-term safety. Vitamin E supplementation improved liver function tests and histological features, particularly in non-diabetic patients. Nevertheless, its use was tempered by potential risks, including cardiovascular concerns and prostate cancer associations in long-term studies. Emerging therapies targeting pathways such as glucagon-like peptide-1 (GLP-1) receptors and farnesoid X receptors also showed promise but required further validation in larger, long-term trials [13].

The comparative analysis revealed that lifestyle interventions had broader systemic benefits, including cardiovascular risk reduction and metabolic improvements, which were not consistently replicated by pharmacological therapies. However, pharmacological agents played a vital role in cases where lifestyle modifications alone were insufficient or where significant fibrosis warranted aggressive management [14]. The synergistic approach of combining lifestyle changes with medications appeared to be the most effective strategy in improving outcomes for patients with moderate to severe NAFLD.

Another notable finding was the heterogeneity of patient responses, underscoring the need for personalized treatment approaches. Factors such as age, baseline metabolic health, severity of liver disease, and genetic predispositions influenced treatment efficacy [15]. For instance, patients with advanced fibrosis derived more benefit from pharmacological therapies, while those in earlier stages responded well to lifestyle changes. The study highlighted the importance of tailoring interventions based on individual patient profiles and disease severity [16-18].

Despite the promising results, the study had limitations. The relatively short follow-up period may not have captured the long-term benefits or adverse effects of either intervention. Additionally, the variability in adherence to lifestyle recommendations introduced potential biases, as did the heterogeneity of pharmacological regimens across studies [19]. Future research should focus on longer-term trials, exploring the integration of digital health tools and structured behavioral support to enhance adherence to lifestyle modifications. Moreover, investigating the cost-effectiveness of these approaches will be critical, given the growing global burden of NAFLD.

In conclusion, this study reaffirmed the foundational role of lifestyle interventions in managing NAFLD while acknowledging the complementary role of pharmacological therapies, particularly in advanced cases. A tailored, patient-centric approach combining both strategies offers the greatest potential for mitigating the burden of this increasingly prevalent condition [20].

CONCLUSION:

This study demonstrated that both lifestyle interventions and pharmacological therapies significantly impacted the management of Non-Alcoholic Fatty Liver Disease (NAFLD). Lifestyle modifications, including dietary adjustments and increased physical activity, proved effective in reducing hepatic fat and improving metabolic parameters. Pharmacological therapies offered additional benefits, particularly for patients with more advanced disease or those unable to sustain lifestyle changes. However, the combination of lifestyle and pharmacological approaches yielded the most favorable outcomes. These findings underscored the importance of a personalized treatment strategy to optimize patient outcomes in NAFLD management. Further research was recommended to refine these interventions.

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