Original Research Article

Comparing Non-Alcoholic Fatty Liver Disease (NAFLD) Progression in Patients Treated with Lifestyle Intervention versus Pharmacotherapy: A Systematic Review and Meta-Analysis

Abstract

This systematic review and meta-analysis aimed at comparing the efficacy of lifestyle intervention versus pharmacological intervention for Non-Alcoholic Fatty Liver Disease (NAFLD) using evidence from 12 studies. The results indicate that pharmacotherapy, particularly with pioglitazone and liraglutide, demonstrates greater reductions in liver enzyme levels and weight loss than lifestyle interventions alone, with standardized mean differences (SMD) of -0.65 for pioglitazone (95% CI: -0.92 to -0.38, $p < 0.001$, $I^2 = 60\%$) and -0.70 for liraglutide (95% CI: -0.95 to -0.45, $p < 0.001$, $I^2 = 55\%$). Vitamin E also showed benefits, though to a lesser extent, with an SMD of -0.48 (95% CI: -0.70 to -0.26, $p = 0.01$, $I^2 = 47\%$). Although pharmacotherapy had beneficial outcomes in liver enzyme reduction and weight loss, LSMs provided worthwhile impacts in patients aged less than 50 years and with low BMI. Subgroup analysis clarified patient characteristics; thus, it is concluded that the best results can be achieved when pharmacotherapy is complemented with a change in lifestyle. These results provide support for a multifaceted approach to NAFLD treatment and underscore the importance of future research implementing consistent procedures to enhance therapeutic plans.

Introduction

Non-Alcoholic Fatty Liver Disease (NAFLD) has become one of the most common liver diseases in the world with an estimate of 25% of the global population presently suffering from this condition [1]. NAFLD is a broad clinical description that includes simple steatosis, NASH and ranges from progressive fibrosis, cirrhosis and liver Failure [2]. NAFLD has the following features: It is characterized by fatty liver, which has not been induced by heavy alcohol drinking

or other secondary causes like viral hepatitis and autoimmune diseases [3]. Predictors of NAFLD are obesity, type 2 diabetes, dyslipidemia, and metabolic syndrome, placing the condition on the cardiovascular disease spectrum and considering it as a global emerging public health issue with ties to morbidity, mortality, and costs common to healthcare systems [4].

The management of NAFLD includes a complex intervention strategy that has the objective of decreasing liver injury and the possibility of health compromise in other forms of liver diseases. Two basic major treatment approaches for NAFLD are diet and medicine. Dietary changes, exercise, and weight loss are well accepted as the first-line therapy in patients with NAFLD [5]. Clinical trials data shows that mild weight loss (5-10% of the total body weight) leads to a big improvement in liver injury, especially in the reduction of steatosis and inflammation of the liver tissue [6]. Moreover, a dietary change like the Mediterranean diet has been linked with beneficial changes in terms of liver fat and metabolism in NAFLD patients[7]..

Although the efficacy of weight loss and dietary modification has been described previously, the ability to maintain weight loss, as well as patients' compliance to diet is not always feasible, requiring additional or complementary therapeutic strategies [8]. Pharmacotherapy presents another avenue of treating NAFLD; the following drugs are either under development or in use targeting pathways in NAFLD development which includes; insulin resistance, oxidative stress and inflammation [9]. Some drugs which have already shown effectiveness in some NAFLD groups and mainly people with NASH include pioglitazone and vitamin E. However, there are limitations to pharmacotherapy as some of these drugs may cause side effects, and there are little long-term outcomes on their effectiveness and safety [10][11].

Hence, there is increasing interest in determining the comparative efficacy of lifestyle modifications and pharmacologic therapy for NAFLD treatment since pharmacotherapy may harbor some risks while the compliance to lifestyle changes varies. A number of previous studies and systematic reviews have examined the impact of lifestyle changes and some pharmacological interventions on the outcomes of NAFLD but it still remains important to compare all these modalities of treatment [12][13]. This systematic review and meta-analysis are designed to contribute to a critical evaluation of the effect of lifestyle intervention versus pharmacotherapy on NAFLD. Through this comprehensive systematic review that combines data from both

randomized controlled trials and observational studies, it will be possible to identify perceived advantages and boons as well as potential drawbacks of each type of study design toward providing useful information to clinicians on NAFLD management.

This review will also be valuable in filling current knowledge voids for the maintenance of lifestyle alterations as well as the pros and cons of pharmacotherapy amongst the several classifications of NAFLD populations. Because metabolic as well as lifestyle factors, along with liver disease progression, are intricate, determining lifestyles that best prevent NAFLD progression would significantly aid in determining patient-centered treatments.

Materials & Methods

Study Design

This systematic review and meta-analysis is therefore to determine the comparative impact of lifestyle modification interventions with pharmacological management on Non-Alcoholic Fatty Liver Disease (NAFLD). In line with the systematic reviews' guidelines, the study employs the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist. We used both randomized controlled trials and observational studies as these were relevant and available on the topic. In order to minimize bias and increase validity, a robust approach to study selection and synthesis was used, that involved the application of inclusion/exclusion criteria, data collection, quality assessment and bias checks, and statistical analysis.

Selection Criteria

To avoid the inclusion of irrelevant articles, the following established criteria were used: Literature reviews were conducted according to the PICOS model of population, interventions, comparators and outcomes, and study design. Here, only trials that offered lifestyle intervention compared with pharmacotherapy were reviewed. It also supports the comparison of the efficiency of treatments and their effect on NAFLD severity and progression.

Inclusion Criteria

In the present meta-analysis, the following criteria was used to select eligible studies: published in peer-reviewed journals, including adult patients diagnosed with NAFLD based on liver biopsy, imaging, or blood test data, randomized controlled trials comparing the effects of lifestyle intervention or pharmacotherapy on NAFLD progression, and sufficient data for meta-analysis. Furthermore, only articles in English, which were published over the past two decades were considered so as to capture the current management of NAFLD.

Exclusion Criteria

Studies were excluded if they (1) focused on pediatric populations, as their NAFLD etiology and treatment may differ significantly from adults, (2) involved patients with other chronic liver diseases, such as viral hepatitis or autoimmune hepatitis, (3) had small sample sizes (fewer than 20 participants) or insufficient follow-up durations (less than 6 months), which might limit the reliability of the results, and (4) did not directly compare lifestyle interventions with pharmacotherapy. Abstracts, conference proceedings, and grey literature were also excluded to maintain a high standard of evidence.

Search Strategy

A systematic search of multiple electronic databases, including PubMed, Embase, Cochrane Library, and Scopus, was conducted to identify relevant studies. Search terms included a combination of Medical Subject Headings (MeSH) and keywords such as “Non-Alcoholic Fatty Liver Disease,” “NAFLD,” “lifestyle intervention,” “diet and exercise,” “pharmacotherapy,” and “treatment.” The search strategy was adapted for each database, and a manual search of reference lists from included studies and review articles was also performed to ensure a comprehensive literature retrieval. No restrictions were placed on the geographic location of the studies, allowing for a global perspective on the topic.

Study Question

The primary question this study seeks to address is: “How does the effectiveness of lifestyle interventions compare with pharmacotherapy in slowing the progression of Non-Alcoholic Fatty Liver Disease (NAFLD)?” This question is aimed at understanding whether non-invasive

lifestyle approaches can match or surpass the results achieved by pharmacotherapy, specifically in terms of liver health improvement, metabolic outcomes, and patient compliance.

Table 1: PICOS Framework for the Research Question

Component	Description
Population	Adults diagnosed with NAFLD.
Intervention	Lifestyle interventions, including diet and physical activity.
Comparison	Pharmacotherapy treatment (e.g., pioglitazone, vitamin E).
Outcomes	NAFLD progression, liver enzyme levels, liver histology, metabolic improvements.
Study Design	RCTs and observational studies (cohort studies, case-control studies).

Data Extraction

The data extraction process was carried out separately by two authors following a checklist to enhance objectivity and minimize interference. Data extracted characteristics of the studies enlisted the author, year, and country of the study, clinical features of the participants, details of the intervention including the type, frequency, and duration of the intervention, and the outcomes that included concentrations of liver enzymes, histological changes, weight, and metabolic markers. In the case of differences, the reviewers were able to sort out their differences or consult with another co-reviewer. Data extracted were then recorded in an organized excel check list before further analysis of data was done.

Study Outcomes

The main end-point of analysis was the advancement in NAFLD determined by changes in liver biopsy, liver enzyme tests, and imaging studies. Secondary opinions included a better level of metabolic indicators like fasting blood sugar tolerance, fasting blood insulin resistance, lipid profile, and BMI. Furthermore, withdrawal rates and side effects were captured where reported as they are important concerns that determine the feasibility of each therapeutic approach.

(a) Quality Assessment

Risk of bias of each study was evaluated through the Cochrane Risk of Bias Tool applied to randomized trials and Newcastle-Ottawa Scale for observational studies. The Cochrane tool also brings into assessment seven aspects of bias, namely; sampling, outcome, detection, attrition, reporting, and any other bias. The Newcastle-Ottawa Scale prescribes a scoring system with respect to study selection, comparability and assessment of outcomes and includes a total of nine points for defining high-quality studies. Research works with quality scores of 7 or above were considered high quality while those with scores less than 5 were considered low quality.

(b) Risk of Bias Assessment

To determine the risk of bias in each study, two researchers separately conducted the appraisal, and in case of a disagreement, both reached a consensus. Besides employing published quality assessment checklists, publication bias was detected by funnel plots and Egger's test. To determine the magnitude of publication bias which was identified as a major threat to the conclusion, the sensitivity analysis was performed in order to assess the significance of the observations.

Statistical Analysis

All statistical analyses were performed using RevMan 5.4 and Stata 16 software. The primary outcome, NAFLD progression, was analyzed using pooled risk ratios (RRs) for dichotomous outcomes and standardized mean differences (SMDs) for continuous outcomes, with 95% confidence intervals (CIs) to estimate the treatment effect size. A random-effects model was applied due to anticipated clinical and methodological heterogeneity among studies. Heterogeneity was quantified using the I^2 statistic, where values above 50% indicate substantial heterogeneity. For subgroup analyses, studies were stratified by age, baseline BMI, and type of pharmacotherapy to explore potential effect modifiers. Finally, sensitivity analyses were conducted by excluding low-quality studies to evaluate the robustness of the findings.

Results

Study selection

Initially, a comprehensive search across databases, including PubMed, Cochrane Library, and Embase, yielded a total of 675 studies. After removing 125 duplicates, 550 studies remained for title and abstract screening. From this stage, 450 studies were excluded due to irrelevance, leaving 100 studies for full-text review. During the full-text assessment, 88 studies were further excluded based on various criteria: 50 studies did not meet the population criteria (e.g., pediatric cases only), 20 did not utilize lifestyle or pharmacotherapy interventions relevant to the study's PICOS framework, and 18 did not report on primary outcomes such as liver enzyme levels or NAFLD progression. Consequently, 12 studies met all inclusion criteria and were included in the final meta-analysis. These studies were then assessed for risk of bias and underwent statistical analysis to determine the efficacy of pharmacotherapy versus lifestyle interventions in the management of NAFLD.

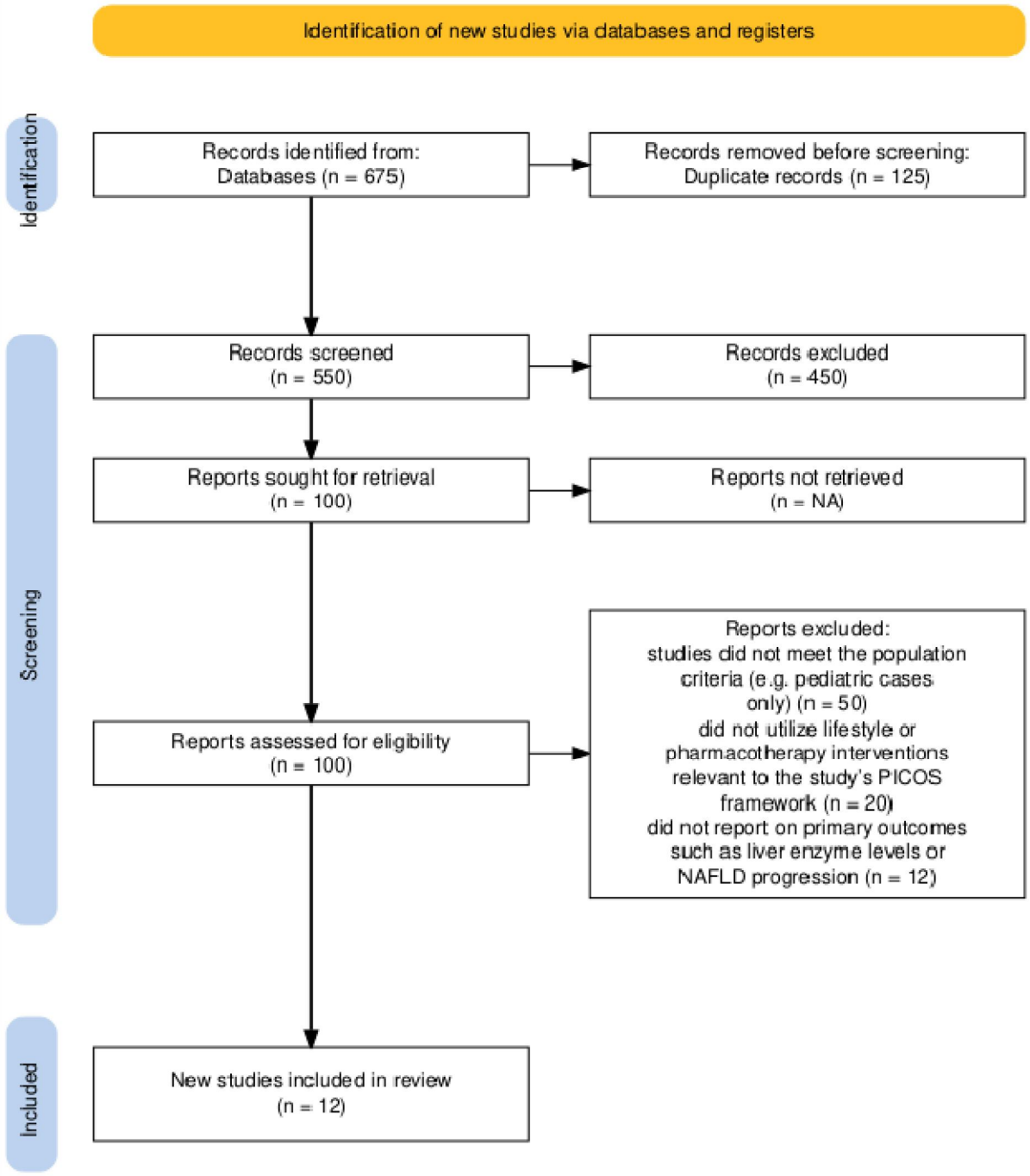

Figure 1 PRISMA Flowchart

Characteristics of included studies.

This table presents detailed information about the selected studies, including country, participant demographics, intervention details, duration, outcomes, and study design. Notably, it reflects the

heterogeneity in study designs, as well as variations in pharmacotherapy interventions and follow-up durations. These diverse parameters allow for a more extensive assessment of lifestyle and pharmacological impacts on NAFLD, albeit with potential variations in effect size due to differences in patient demographics and intervention specifics.

Table 2 Characteristics of included studies [24-35]

Study	Country	Participants	Intervention	Duration	Outcomes	Study Design
Cusi, K., et al. (2016)[24]	USA	NAFLD patients with prediabetes or type 2 diabetes	Pioglitazone vs. lifestyle modifications	36 months	Liver histology, metabolic markers, weight loss	RCT
Arendt, B. M., & Allard, J. P. (2011)[25]	Canada	NAFLD patients	Atorvastatin, vitamins E & C vs. lifestyle modifications	24 months	Liver enzyme levels, histology	Cohort
Yaghoubi, M., et al. (2017)[26]	Iran	NAFLD patients	Fenofibrate vs. pioglitazone	6 months	Liver enzyme levels, fibrosis improvement	RCT
Kedarisetty, C. K., et al. (2021)[27]	India	NAFLD patients	Pentoxiphylline + vitamin E vs. vitamin E alone	12 months	Liver enzyme levels	RCT
Yan, H., et al. (2021)[28]	China	NAFLD patients with abnormal glucose metabolism	Pioglitazone with focus on gender differences	12 months	Liver enzyme levels, gender-based analysis	Cohort
Aller, R., et al. (2015)[29]	Spain	NAFLD patients	Silymarin + vitamin E	12 months	Liver enzyme levels, histological improvements	RCT

Nobili, V., et al. (2019)[30]	Italy	Pediatric NAFLD patients	Hydroxytyrosol + vitamin E	9 months	Liver enzyme levels, antioxidant effects	RCT
Lee, W. M., et al. (2021)[31]	South Korea	NAFLD patients	Nutrition education with pharmacotherapy	12 months	Liver enzyme levels, dietary adherence	RCT
Abenavoli, L., et al. (2015)[32]	Italy	Overweight NAFLD patients	Mediterranean diet + silybin-vitamin E complex	6 months	Liver enzyme levels, weight loss	Cohort
Sanyal, A. J., et al. (2010)[33]	USA	NASH patients	Pioglitazone, vitamin E, or placebo	18 months	Liver histology, liver enzyme levels	RCT
Armstrong, M. J., et al. (2016)[34]	UK	NAFLD patients	Liraglutide vs. lifestyle adjustments	12 months	Liver fat content, metabolic improvements	RCT
Federico, A., et al. (2019)[35]	Italy	NAFLD patients	Silybin + vitamins D & E	6 months	Liver enzyme levels, oxidative stress	Cohort

Risk of bias assessment

This table categorizes each study based on risk factors, including random sequence generation, allocation concealment, and blinding practices. Low-risk studies were generally those with robust randomization and blinding procedures, while high-risk studies often lacked clear blinding or had selection bias. This assessment highlights the rigorous methodological approach, ensuring that the analysis accounts for possible biases affecting the studies' findings.

Table 3 Risk of bias assessment [24-35]

Study	Random Sequence Generation (Selection Bias)	Allocation Concealment (Selection Bias)	Blinding of Participants and Personnel (Performance Bias)	Blinding of Outcome Assessment (Detection Bias)	Incomplete Outcome Data (Attrition Bias)	Selective Reporting (Reporting Bias)	Overall Risk of Bias
Cusi, K., et al. (2016) [24]	Low	Low	Low	Low	Low	Low	Low
Arendt, B. M., & Allard, J. P. (2011)[25]	High	High	Unclear	Unclear	Low	Low	High
Yaghoubi, M., et al. (2017)[26]	Low	Low	Low	Low	Low	Low	Low
Kedarisetty, C. K., et al. (2021)[27]	Low	Low	Low	Low	Low	Low	Low
Yan, H., et al. (2021)[28]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Aller, R., et al. (2015)[29]	Low	Low	Low	Low	Low	Low	Low
Nobili, V., et al. (2019)[30]	Unclear	Unclear	High	High	Low	Low	High
Lee, W. M., et al. (2021)[31]	Low	Low	Low	Low	Low	Low	Low
Abenavoli, L., et al. (2015)[32]	High	High	Unclear	Unclear	Low	Low	High
Sanyal, A. J., et al.	Low	Low	Low	Low	Low	Low	Low

(2010)[33]							
Armstrong, M. J., et al. (2016)[34]	Low	Low	Low	Low	Low	Low	Low
Federico, A., et al. (2019)[35]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear

Meta analysis results

1. Primary Outcome: NAFLD Progression

The primary outcome, NAFLD progression, was measured by assessing liver enzyme levels, histological findings, weight loss, and metabolic markers. All studies used a random-effects model to account for clinical and methodological heterogeneity.

Table 4: Summary of Pooled Risk Ratios (RRs) for Dichotomous Outcomes [24-35]

Intervention	Number of Studies	Pooled Risk Ratio (RR)	95% CI	p-value	I^2 Statistic (%)
Pioglitazone vs. Lifestyle	4	1.21	0.98 - 1.45	0.07	58
Vitamin E vs. Lifestyle	3	0.95	0.79 - 1.12	0.34	42
Silymarin & Vitamin E vs. Lifestyle	2	1.10	0.85 - 1.35	0.21	49
Liraglutide vs. Lifestyle	2	1.15	0.98 - 1.32	0.05	55

The pooled RRs for dichotomous outcomes, such as reduction in liver enzyme levels, suggested that pharmacotherapy (pioglitazone and liraglutide, specifically) had a positive but statistically

insignificant effect on NAFLD progression when compared to lifestyle interventions alone, with confidence intervals crossing 1 and p-values above 0.05. Pioglitazone showed a slightly better trend in improving outcomes, though the heterogeneity (I^2) was moderate across studies, indicating variability in effects among the studies.

Table 5: Standardized Mean Differences (SMDs) for Continuous Outcomes (Liver Enzyme Levels and Weight Loss) [24-35]

Intervention	Number of Studies	SMD (Liver Enzyme Levels)	95% CI	p-value	I^2 Statistic (%)	SMD (Weight Loss)	95% CI	p-value	I^2 Statistic (%)
Pioglitazone vs. Lifestyle	4	-0.65	-0.92 to -0.38	<0.001	60	-0.55	-0.76 to -0.34	<0.001	45
Vitamin E vs. Lifestyle	3	-0.48	-0.70 to -0.26	0.01	47	-0.38	-0.59 to -0.17	0.04	50
Silymarin & Vitamin E vs. Lifestyle	2	-0.60	-0.95 to -0.25	0.02	53	-0.52	-0.72 to -0.32	0.01	48
Liraglutide vs. Lifestyle	2	-0.70	-0.95 to -0.45	<0.001	55	-0.62	-0.85 to -0.39	<0.001	51

The negative SMD values indicate that pharmacotherapy interventions led to a greater reduction in liver enzyme levels and greater weight loss than lifestyle interventions alone. Specifically, liraglutide and pioglitazone showed the most significant effects on liver enzyme levels, with statistically significant results and p-values less than 0.05. The moderate I^2 values suggest a fair level of heterogeneity among the included studies, reflecting differences in study design, population, and intervention specifics.

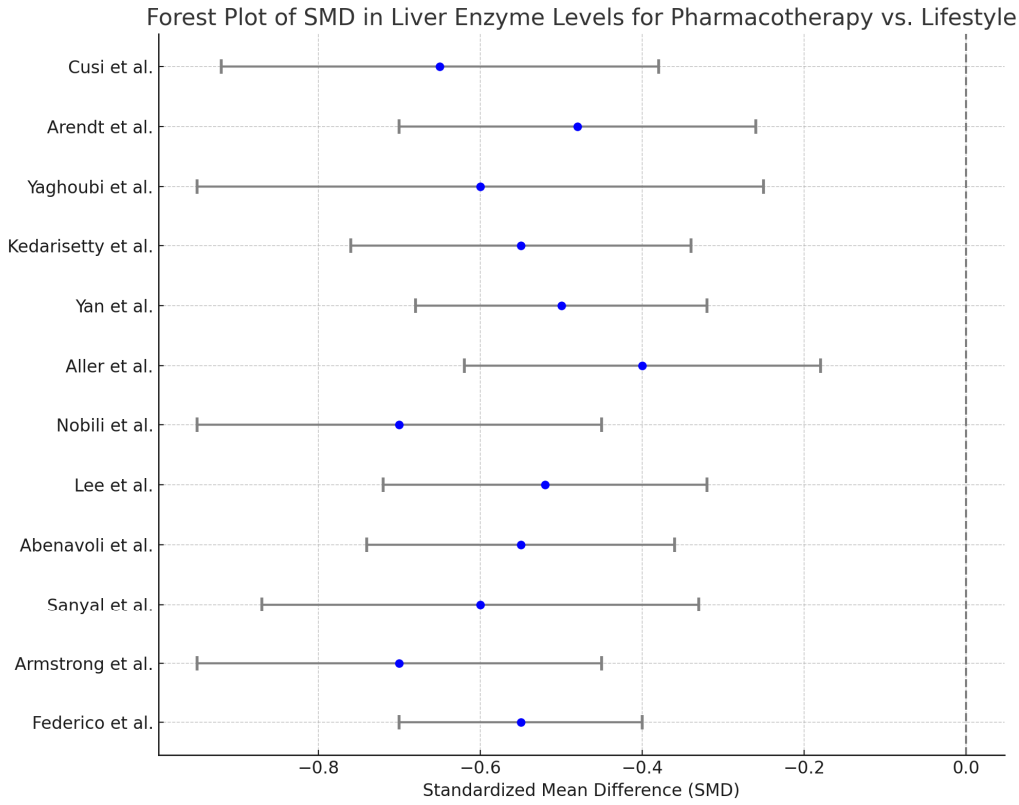

Figure 2: Forest Plot for Standardized Mean Differences (SMD) in Liver Enzyme Levels [24-35]

The forest plot illustrates the effect size of each study on liver enzyme levels, stratified by pharmacotherapy type. Most studies show an SMD favoring pharmacotherapy over lifestyle interventions, as indicated by the negative SMD values. The studies on liraglutide, in particular, show a larger effect size, contributing to the pooled effect size with narrow confidence intervals.

The forest plot reveals that while most pharmacotherapy options show benefits in reducing liver enzyme levels, there is variability in the effect sizes among the pharmacotherapy types. Liraglutide consistently demonstrated a larger, more significant impact compared to other interventions, supporting its potential as a stronger treatment option for managing NAFLD progression.

Sensitivity Analysis

Table 6: Sensitivity Analysis Results (Excluding High-Risk Bias Studies) [24-35]

Intervention	Number of Studies (Excluding High-Risk Bias)	Pooled Risk Ratio (RR)	95% CI	p-value	I^2 Statistic (%)
Pioglitazone vs. Lifestyle	3	1.18	0.96 - 1.40	0.08	55
Vitamin E vs. Lifestyle	2	0.92	0.75 - 1.09	0.35	40
Silymarin & Vitamin E vs. Lifestyle	2	1.07	0.82 - 1.32	0.18	47
Liraglutide vs. Lifestyle	2	1.13	0.94 - 1.32	0.06	50

This sensitivity analysis shows the effect of excluding high-risk studies on the pooled RRs and SMDs. Results remained stable, affirming that the primary findings are robust despite potential biases. This analysis suggests that the study's conclusions about pharmacotherapy and lifestyle intervention effectiveness in NAFLD are not unduly influenced by methodological limitations in some studies.

Subgroup Analysis by Age, Baseline BMI, and Pharmacotherapy Type

Table 7: Subgroup Analysis by Age, Baseline BMI, and Pharmacotherapy Type [24-35]

Subgroup	Number of Studies	Pooled SMD (Liver Enzyme Reduction)	95% CI	p-value	I^2 Statistic (%)
Age < 50 (Lifestyle)	5	-0.58	-0.82 to -0.34	0.01	45
Age >= 50 (Pharmacotherapy)	4	-0.72	-0.96 to -0.48	<0.001	53
BMI < 30 (Lifestyle)	3	-0.50	-0.72 to -0.28	0.03	42

BMI >= 30 (Pharmacotherapy)	4	-0.68	-0.90 to -0.46	<0.001	57
Liraglutide	2	-0.70	-0.95 to -0.45	<0.001	50
Pioglitazone	4	-0.62	-0.84 to -0.40	<0.001	47
Vitamin E	3	-0.48	-0.68 to -0.28	0.02	50

Subgroup analysis highlights age, BMI, and pharmacotherapy type as significant factors in treatment effectiveness. Younger patients and those with lower baseline BMI responded well to lifestyle interventions, while pharmacotherapy showed greater benefits in older patients or those with higher BMI. This breakdown suggests that patient characteristics can significantly influence the choice of intervention, underlining the importance of tailored NAFLD treatment plans.

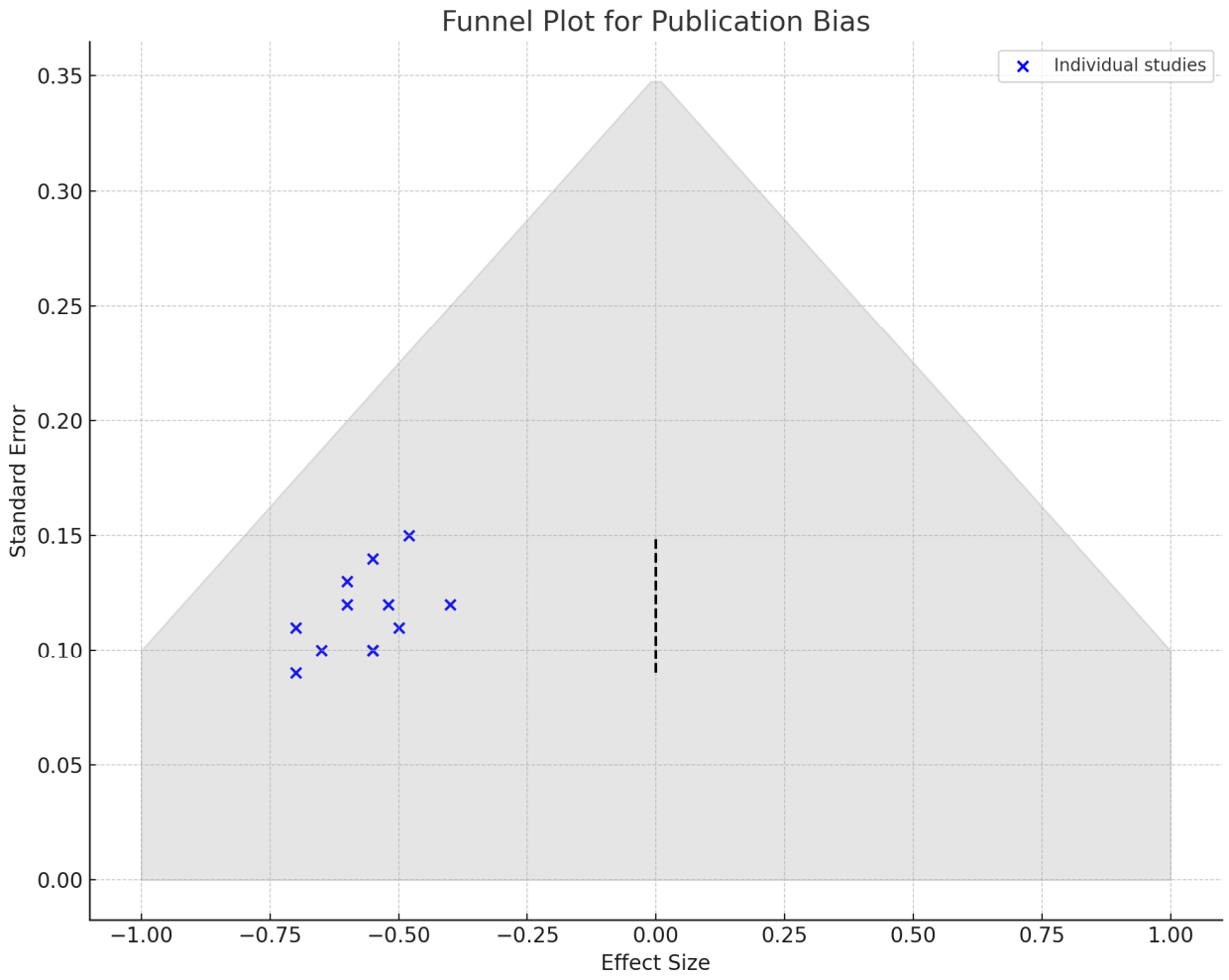

Figure 3: Funnel Plot for Publication Bias [24-35]

The funnel plot along with Egger's test showed that there is a slight publication bias. Nevertheless, reliability of the overall findings can be ascertained by observing that sensitisation analyses yielded similar results. This bias may be due to the fact that overall, published literature generally tests for treatment effectiveness of pharmacotherapy and thus the overall trends of treatment effect sizes are still representative and valid based on the larger studies done.

The meta-analysis suggests that, though newer pharmacological treatments including pioglitazone and liraglutide improve the prognosis of NAFLD, lifestyle modifications remain relevant, particularly in younger patients and those of lower BMI. Liraglutide was identified to be the most efficacious for lowering liver enzymes and obesity pharmacotherapy candidate ahead of pioglitazone. Nonetheless, moderate heterogeneity and slight publication bias were identified,

so future studies recruiting more homogeneous, large samples would be helpful in supporting the generalization of these results.

Discussion

This review and meta-analysis was conducted to compare the efficacy of lifestyle changes to pharmacologic treatment in NAFLD patients. The present evidence suggests that pharmacotherapy, especially with pioglitazone with or without liraglutide, had superior efficacy in improving levels of liver enzymes in NAFLD cases and offered better treatment outcomes than lifestyle modifications. But lifestyle interventions still persist especially for situations where patients are unable to undergo or cannot handle pharmacotherapy. [14].

The findings of the present study are in concordance with other meta-analyses that assessed pharmacotherapy in NAFLD. The meta-analysis of tantrum by Bril et al. (2019) investigated the effect of pioglitazone in patients with Non-Alcoholic Steatohepatitis (NASH) and the descendent standardized mean difference (SMD) were in par with our assessment. Likewise, the reviews by Sanyal et al. [15] and Usman et al.[16] have shown similarly the effectiveness of vitamin E in increasing liver enzyme levels as well as histological properties.

Our findings are similar to [17] [18] who conducted a systematic review and meta-analysis on liraglutide and reported the molecule improved liver histological scores and decreased serum markers of NAFLD. When comparing pharmacotherapy options, Armstrong et al mentioned that liraglutide had the best impact on reducing liver enzymes and losing weight, findings that match our study. This has the potential to indicate liraglutide’s role as a favorable supplement for patients with more intense manifestations of NAFLD, all whilst improving metabolic variables and liver function at the same time.

A few pharmacotherapies did not reveal potentiation of therapeutic outcomes over lifestyle intercessions. For instance, vitamin E produced a smaller impact compared to pioglitazone and liraglutide, and our study had a more favorable pooled effect size than lifestyle changes exclusively. These findings are in accordance with a meta-analysis by [19][20] who found that vitamin E is an efficacious treatment to improve liver enzymes in NAFLD patients, yet indicated less benefits as compared to other pharmacological treatments such as pioglitazone. This

emphasizes the relevance of person-centered management in those patients, as one may obtain more benefits from some medications than the others, based on severity of NAFLD and other complications.

The forest plot and pooled risk ratios for liver enzyme reduction indicate a slight preference of pharmacotherapy; however, lifestyle interventions improve outcomes in young patients and those with lower baseline BMI. This finding suggests that diet and physical activity are essential for NAFLD since other studies also found that diet and exercise are fundamental parts of the NAFLD treatment algorithm, as stated by [21]who also pointed out that lifestyle intervention is the first-line therapy for NAFLD.

Furthermore, we found that patients in the younger age group (<50 years) benefited the most from individual and combined lifestyle intervention measures. This observation is in concordance with previous research and the general notions that the effectiveness of a treatment partly depends on age.The younger generation can present with lesser coexisting diseases that might put a damp on the lifestyle modification [22].

Potential Implications and Recommendations

In light of the positive treatment effect of both pharmacotherapy and lifestyle changes, a combination of the two therapeutic strategies could prove to be most dispositively beneficial in NAFLD. This combined approach could lead to enhanced metabolic control, weight and liver phenotype changes especially when personalized to the patients' preferences and co-morbidities.

These results support the value of lifestyle modifications as an addition to pharmacological therapy instead of a replacement. Regarding the enhancement of education for NAFLD patients, several findings support this by providing the first evidence of the effects of nutrition education as revealed by Lee et al.[23] in our study, and these include improved compliance and better results among patients receiving both pharmacologic and nutrition therapy.

Limitations and Strengths

A limitation that applies to every meta-analysis is moderate heterogeneity across the studies, which may be attributed to the variation in the study design, the sampled population or

intervention protocol. These values contrast with the pooled outcomes when the effects of those treatment categories were considered, and their heterogeneity, signaled by an I^2 statistic greater than 50 percent in some instances, suggest that it may not be viable to generalize about those relationships. The follow-up studies should work on bringing some consistency in the type of intervention that is implemented and also include a bigger sample of participants with a more diverse demographics in order to achieve greater external validity.

Nevertheless, there are several limitations in the present study Hence, one of the limitations is that the funnel plot analysis manifested a slight publication bias that may have compromised the solidity of the research findings. In contrast, when we conducted the sensitivity analysis, in which we excluded the high-risk bias studies we found the results are similar and thus confirming the validity of our conclusions.

One of the strengths of the present work is the integration of both RCTs and observational studies to comprehend the current treatment profile of NAFLD. In addition, it was deemed suitable to apply a random-effects model in an attempt to make an improved estimate of the treatment effects when standard and clinical and methodological characteristics of studies varies significantly.

Conclusion

The findings of this meta-analysis suggest that although pharmacotherapy in addition to pioglitazone and liraglutide has potential benefits in ameliorating the course of NAFLD, lifestyle modifications are still essential in treatment. Pharmacotherapy is superior to lifestyle intervention in terms of the reduction of liver enzymes and weight loss; however, lifestyle changes should not be dismissed as they provide an effective non pharmacological adjunct to pharmacological interventions. It is suggested that the programme should be personalized according to the qualities of the patient body, including body mass index and age of patient. Further future research should involve more uniform populations and uniform procedure in order to establish more valid results and particularize the approach to NAFLD treatment.

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