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Impact of Supervised and Structured Diet and Exercise in Management of Patients with Metabolic Dysfunction Associated Steatohepatitis– A Randomized Controlled Trial

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ABSTRACT

Background: Metabolic Dysfunction Associated Steatohepatitis (MASH) represents the progressive, inflammatory form of metabolic dysfunction associated fatty liver disease (MAFLD), which has emerged as a global health concern. Given the lack of approved pharmacological treatments for MASH, structured lifestyle interventions involving supervised diet and exercise have gained attention.

Objective: To evaluate the impact of a supervised and structured dietary and physical activity intervention on liver health, metabolic parameters, and anthropometric indices in newly diagnosed MASH patients.

Methods: A randomized controlled trial was conducted among 188 first-time diagnosed MASH patients at KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. Participants were randomly assigned to either a study group (supervised structured diet and exercise regimen) or a control group (standard care). Anthropometry, liver function tests, lipid profile, and FibroScan parameters were recorded at baseline and 24 weeks. The intervention included a calorie-restricted Mediterranean diet, aerobic exercise (30–45 minutes/day for 5 days/week), and weekly telephonic follow-up.

Results: Participants in the intervention group demonstrated statistically significant improvements across all measured parameters over 24 weeks. Notable reductions were observed in weight (↓11.41 kg), BMI (↓3.73 kg/m²), waist circumference (↓3.69 cm), AST (↓20.27 U/L), ALT (↓32.35 U/L), triglycerides (↓99 mg/dL), CAP score (↓61.89 dB/m), LSM (↓4.05 kPa), FIB-4 (↓0.22), and APRI (↓0.12) ($p < 0.05$ for all). Post-intervention, 86.1% of participants in the intervention group attained "good" health practice scores compared to 15% in the control group.

Conclusion: Supervised and structured dietary and exercise interventions significantly improved clinical and biochemical markers in MASH patients. Incorporating such lifestyle modifications into routine care may mitigate disease progression and improve long-term outcomes.

Keywords: *MAFLD, MASH, Lifestyle Intervention, FibroScan, CAP score, Liver Stiffness Measurement, Mediterranean Diet.*

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1. INTRODUCTION

Metabolic Dysfunction Associated Steatohepatitis (MASH), a progressive subtype of metabolic dysfunction associated fatty liver disease (MAFLD), is becoming an alarming global health concern due to its association with obesity, metabolic syndrome, and type 2 diabetes mellitus (T2DM) (1). MAFLD itself is characterized by the accumulation of hepatic fat in individuals without significant alcohol intake or other known causes of liver disease. It encompasses a spectrum ranging from simple steatosis (Metabolic Dysfunction Associated Fatty Liver Disease- MAFLD) to MASH, fibrosis, cirrhosis, and eventually hepatocellular carcinoma (HCC) (2). In this spectrum, MASH is a critical turning point due to its potential for irreversible hepatic damage and adverse clinical outcomes.

Recent studies have highlighted the epidemiological importance of MASH in the Indian population (3). A meta-analysis from India indicated that the prevalence of MAFLD ranges from 9% to 53%, with a pooled prevalence of 38.6% among Indian adults (4). Specifically, in North Karnataka, a recent community-based screening study found the incidence of MASH to be 31.23% among the general population, with significant associations noted with obesity, diabetes, and dyslipidemia. Furthermore, a female-centric screening study from the same region revealed a MASH prevalence of 35.13% and demonstrated strong correlations with metabolic syndrome parameters such as raised triglycerides, high BMI, and waist circumference (5).

The pathogenesis of MASH involves multiple metabolic insults, including insulin resistance, oxidative stress, lipotoxicity, and chronic inflammation, culminating in liver injury and fibrosis. Early stages are often asymptomatic, and detection typically occurs only after significant progression. This makes early lifestyle-based intervention a critical strategy in halting disease advancement (3).

Currently, no FDA-approved pharmacotherapy exists for MASH. As a result, international consensus guidelines prioritize lifestyle modification as the cornerstone of MASH management (6). Structured diet and physical activity are considered first-line approaches, aiming to reduce hepatic fat, ameliorate insulin resistance, and attenuate liver inflammation. A sustained weight loss of 7–10% has been shown to significantly improve hepatic steatosis and fibrosis. However, one of the key challenges is ensuring adherence to lifestyle change, which is often suboptimal in unsupervised settings (7).

To address these gaps, structured and supervised interventions particularly those incorporating evidence-based dietary patterns such as the Mediterranean diet, along with monitored aerobic exercise are being actively studied (7,8). These regimens are tailored to ensure higher compliance and consistency through professional support, mobile tracking tools, and periodic reinforcement. Such supervised programs not only ensure accurate implementation but also enhance patient motivation, leading to sustainable behavioral change (9).

In the present randomized controlled trial, we hypothesized that a well-structured and closely monitored lifestyle intervention would significantly improve clinical and biochemical parameters in patients diagnosed with MASH. The study was conducted in a real-world tertiary care setting in North Karnataka, making it regionally relevant and potentially impactful for public health guidelines in similar Indian populations. Outcomes were evaluated using validated non-invasive diagnostic tools like FibroScan (LSM and CAP), FIB-4, APRI, and biochemical liver markers.

This study aims to bridge the gap between the theoretical benefits of lifestyle modification and its practical effectiveness in a supervised format. Through this trial, we seek to generate evidence that can inform future policies for MASH management, including the incorporation of structured lifestyle programs into mainstream medical practice.

2. MATERIALS AND METHODS

Study Design and Setting:

This was a single-center, randomized controlled trial conducted at the Gastroenterology OPD of KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. The study was registered with CTRI (CTRI/2022/02/040411) and approved by the Institutional Ethics Committee (Ref. No. KAHER/EC/21-22/014).

Inclusion criteria:

Age 18–55 years

Newly diagnosed MASH confirmed by elevated LFTs or raised FibroScan values (CAP >238 dB/m, LSM 7.1–14 kPa)

Exclusion criteria:

Alcohol use

Use of hepatotoxic drugs

History of malignancy, diabetes, cardiovascular instability

Participation in another trial in past 3 months

Sample Size and Randomization

A total of 188 subjects were recruited using simple random sampling (envelope method) and equally distributed into control and intervention groups.

Intervention Protocol

Control Group:

Received standard counseling for diet and exercise through five face-to-face sessions

Intervention Group:

Underwent supervised lifestyle modification including:

Mediterranean-style diet with 30% caloric restriction to promote 7–10% weight loss

Aerobic exercises (brisk walking, cycling, swimming) for 30–45 minutes, 5 days/week

Weekly telephonic monitoring and digital tracking via fitness bands and mobile apps

Outcome Measures

Parameters were measured at baseline and at 24 weeks:

Anthropometry: Weight, BMI, waist circumference

Biochemical: AST, ALT, Triglycerides

FibroScan Parameters: CAP score (steatosis), LSM (fibrosis)

Fibrosis Scores: FIB-4, APRI

Health Practices: 30-item questionnaire converted to percentage scores:

≤50%: Poor

51–75%: Average

≥76%: Good

3. STATISTICAL ANALYSIS

Data were analyzed using SPSS and Microsoft Excel. Continuous variables were analyzed using t-tests and repeated measures ANOVA. A p-value <0.05 was considered statistically significant.

Table 1: CAP Score Categories and Steatosis Grade

CAP Score (dB/m)	Steatosis Grade	% of Liver with Fat
238–260	S1	11%–33%
260–290	S2	34%–66%
>290	S3	≥67%

Purpose: Used to classify the extent of hepatic steatosis in patients.

Context: Explains how FibroScan-derived CAP scores were interpreted during the assessment of participants.

Placement: Belongs in the Materials and Methods section under the subheading "FibroScan Interpretation Criteria" or similar.

Table 2: CAP and LSM Score Criteria for MAFLD Spectrum

Disease Condition	CAP Score (dB/m)	LSM Score (kPa)
MAFLD (Fatty Liver)	>238	<7
MASH	>238	7.1–14
Cirrhosis	>238	>14

Purpose: Defines diagnostic criteria used to categorize MAFLD, MASH, and Cirrhosis.

Context: Shows how patients were classified based on their CAP and LSM values.

Placement: Also belongs in the Materials and Methods section under "Diagnostic Classification Criteria" or similar.

4. RESULTS

The table shows both frequency counts and percentages for each category. the distribution of gender, age groups, education, occupation, and marital status across intervention group of 188 participants.

Table 3: Demographic variables of the Study Population.

Demographic Variable	Category	Frequency (n=188)	Percentage (%)
Gender	Male	100	53.2
	Female	88	46.8
Age Group	≤30 yrs	18	9.6
	30–45 yrs	98	52.1
	>45–55 yrs	72	38.3
Education	Secondary	50	26.6
	Graduate	138	73.4
Occupation	Housewife	47	25.0
	Self-employed	14	7.4
	Private employee	92	48.9
	Government employee	35	18.6
Marital Status	Married	148	78.7
	Unmarried	40	21.3

Graph 1: Demographic variables of the Study Population.

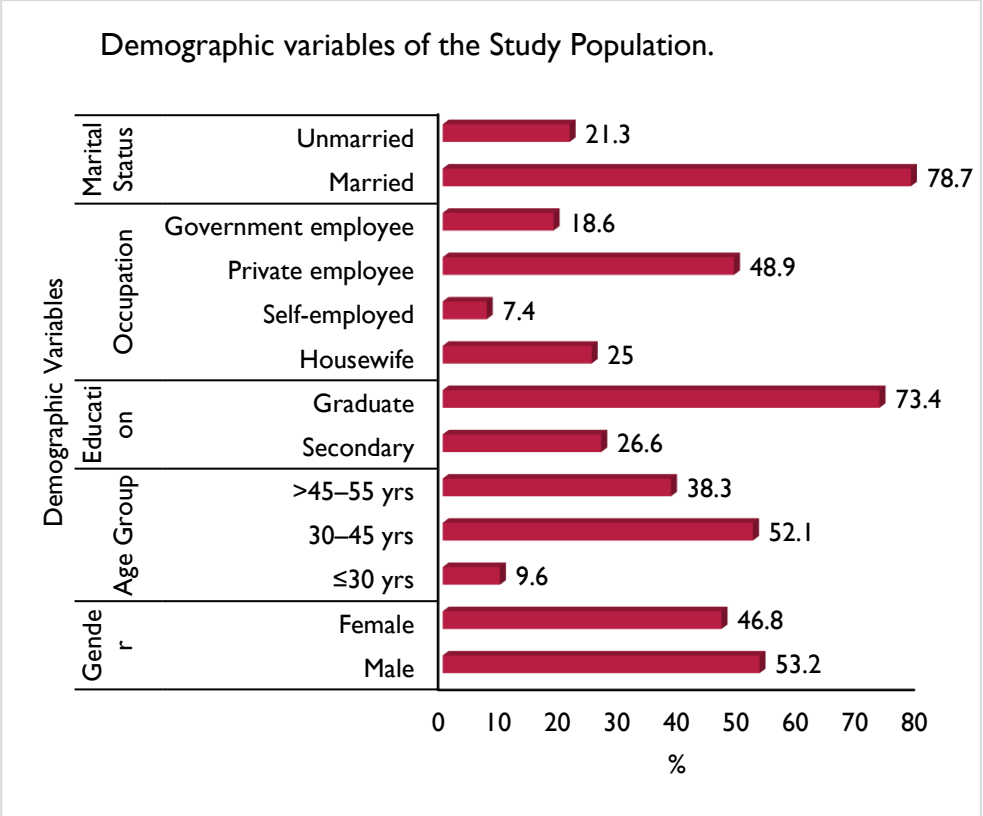

Table 3: The study enrolled a total of 188 newly diagnosed patients with Metabolic Dysfunction Associated Steatohepatitis (MASH). The gender distribution showed a slight male predominance, with 53.2% males and 46.8% females. Most participants (52.1%) were between 30 and 45 years of age, followed by 38.3% aged 46–55 years, and 9.6% were ≤30 years. Educational background indicated that 73.4% were graduates, while 26.6% had completed secondary education. Occupationally, the majority were private employees (48.9%), followed by housewives (25%), government employees (18.6%), and self-employed individuals (7.4%). Marital status showed that 78.7% of participants were married, and the remaining 21.3% were unmarried. This demographic distribution reflects a predominantly middle-aged, educated, and economically active cohort affected by MASH.

Table 4: Comparison of Anthropometric, Biochemical, and Fibroscan Parameters at Baseline and 24 Weeks

Parameter	Time Point	Mean	SD	Mean Difference	p
Waist Circumference (cm)	Baseline	95.47	6.92	↓3.69	< .05
	24 weeks	91.78	6.8		
Weight (kg)	Baseline	82.13	11.99	↓11.41	< .05
	24 weeks	70.72	11.04		
BMI (kg/m²)	Baseline	31.73	4.59	↓3.73	< .05
	24 weeks	28	4.52		
SGOT / AST (U/L)	6 weeks	40.02	8.41	↓20.27	< .05
	24 weeks	19.75	3.87		
SGPT / ALT (U/L)	Baseline	52.96	10.54	↓32.35	< .05
	24 weeks	20.61	3.28		
Triglycerides (mg/dL)	Baseline	241.78	48.15	↓99.00	< .05
	24 weeks	142.78	22.3		
CAP Score (dB/m)	Baseline	277.58	10.81	↓61.89	< .05
	24 weeks	213.17	21.87		
LSM (Fibroscan, kPa)	Baseline	10.96	1.59	↓4.05	< .05
	24 weeks	6.84	1.25		
FIB-4 Index	Baseline	0.63	0.31	↓0.22	< .05
	24 weeks	0.42	0.18		
APRI Index	Baseline	0.27	0.11	↓0.12	< .05
	24 weeks	0.15	0.05		

Table 4: The demonstrated significant improvements in all measured parameters after 24 weeks of intervention. Participants showed marked reductions in weight (↓11.41 kg), BMI (↓3.73), and waist circumference (↓3.69 cm), indicating effective weight loss and central fat reduction. Liver enzymes (AST, ALT) and triglycerides dropped significantly, reflecting improved hepatic function and lipid metabolism. Notably, FibroScan-based CAP scores and liver stiffness measurements (LSM) also declined (↓61.89 dB/m and ↓4.05 kPa respectively), suggesting reversal of hepatic steatosis and fibrosis. FIB-4 and APRI indices also showed favorable regression trends, underscoring the overall clinical benefit of the structured lifestyle intervention.

5. DISCUSSION

The findings of this randomized controlled trial underscore the effectiveness of a structured and supervised lifestyle intervention comprising a calorie-restricted Mediterranean diet and aerobic exercise in improving clinical, biochemical, and hepatic parameters among patients with Metabolic Dysfunction Associated Steatohepatitis (MASH). Over a 24-week period, statistically significant improvements were observed in anthropometric measures, liver enzymes, serum triglycerides, and non-invasive fibrosis markers, confirming the positive impact of the intervention on metabolic health and liver disease progression (10).

A population-based cross-sectional study conducted in Belagavi revealed a 31.23% prevalence of MASH among 730 adults, with a higher burden observed in males (60.52%) and strong associations with obesity, diabetes, and hypertension. Similarly, another large cross-sectional study focusing on female subjects reported a 35.13% prevalence of MAFLD using FibroScan CAP scores ≥275 dB/m, further reinforcing the widespread metabolic burden in this region. These studies also highlighted strong correlations between MASH and elevated BMI, increased waist circumference, and deranged liver function tests, which were also evident in the present study cohortc(11).

The significant post-intervention reductions in BMI (↓3.73 kg/m²) and weight (↓11.41 kg) are particularly important, as a weight reduction of ≥7% has been identified as a threshold for histological improvement in MASH. These findings are consistent with global recommendations that advocate lifestyle modification as the first-line therapeutic strategy for MAFLD and MASH management, especially in the absence of approved pharmacological agents. The reduction in ALT (↓32.35 U/L) and AST (↓20.27 U/L) levels in the intervention group further supports the reversal of hepatic inflammation and necro inflammatory activity (12).

One of the most clinically relevant findings in this trial is the reduction in CAP score (↓61.89 dB/m) and liver stiffness (LSM ↓4.05 kPa), both measured through transient elastography. These reductions indicate regression in both hepatic steatosis and fibrosis severity. The study also tracked fibrosis progression using validated non-invasive indices: FIB-4 and APRI scores. The observed reductions (↓0.22 and ↓0.12 respectively) signal early regression in fibrotic activity.

Another strength of this study was the evaluation of health practices using a structured 30-item questionnaire. Pre-intervention scores indicated poor practices in both groups. However, after the supervised program, 86.1% of the intervention group participants demonstrated “good” health practices compared to only 15% in the control group. This underscores the role of structured supervision, repeated reinforcement, and behavioral tracking in promoting lifestyle adherence elements often missing in routine outpatient counseling.

Collectively, the results from this trial support the feasibility and clinical efficacy of delivering structured, personalized, and supervised interventions in a real-world tertiary care setting. Not only did these interventions reverse steatosis and fibrosis markers, but they also promoted sustainable behavior change, which is pivotal in chronic disease management.

However, the study is not without limitations. The relatively short duration (24 weeks) limits long-term assessment of fibrosis regression and recurrence. Absence of histological confirmation via liver biopsy is another limitation, although justified by the non-invasive design and widespread acceptance of FibroScan as a clinical tool. Additionally, the study did not track dietary macronutrient composition or detailed physical activity adherence using objective metrics beyond fitness bands and telephonic follow-up.

Nonetheless, this trial adds to the growing body of evidence that supports non-pharmacological, lifestyle-first approaches in the management of MASH. In resource-limited settings like India, where access to advanced therapies remains constrained, such structured and supervised lifestyle interventions can serve as a cost-effective, scalable, and impactful model for MAFLD/MASH control at the community level.

6. CONCLUSION

In conclusion, this randomized controlled trial establishes the clinical efficacy of a structured and supervised lifestyle intervention comprising a calorie-restricted Mediterranean diet and regular aerobic exercise in significantly improving anthropometric indices, liver function markers, and non-invasive fibrosis scores among patients with Metabolic Dysfunction Associated Steatohepatitis (MASH). The intervention not only led to reductions in hepatic steatosis and fibrosis as measured by FibroScan but also promoted sustainable improvements in health behavior practices. These findings underscore the critical role of lifestyle modification as a first-line, non-pharmacological approach in managing early-stage MASH, particularly in resource-constrained settings. Incorporating such supervised interventions into standard clinical practice may offer a scalable, cost-effective solution to curb the rising burden of MAFLD and its complications in the Indian population..

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