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RESEARCH ARTICLE

THE EFFECTS OF EXERCISE INTENSITY ON METABOLIC HEALTH IN PATIENTS WITH NAFLD AND TYPE 2 DIABETES: A COMPARATIVE STUDY

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Abstract

Introduction: Non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus (T2DM) are chronic metabolic disorders that are increasingly prevalent globally, posing significant health challenges. Both conditions are linked to obesity, insulin resistance, and sedentary lifestyles, leading to severe complications such as cardiovascular diseases and liver cirrhosis. Exercise is a crucial lifestyle modification that improves metabolic health in these conditions, but the optimal exercise intensity remains debated. This study investigates the effects of different exercise intensities on metabolic health in patients with NAFLD and T2DM to provide insights for tailored exercise prescriptions.

Materials and Methods: This randomized controlled trial involved 100 participants with NAFLD and T2DM, divided into two groups: MICT and HIIT, over 12 weeks. Participants were adults aged 30-65 years with confirmed NAFLD and T2DM, and a sedentary lifestyle. Exclusion criteria included other liver diseases, uncontrolled hypertension, severe diabetic complications, recent participation in a structured exercise program, and contraindications to exercise. Participants were randomly assigned to MICT or HIIT, with exercise sessions supervised by certified physiologists. Primary outcomes were liver fat content and insulin sensitivity, while secondary outcomes included lipid profiles, inflammatory markers, feasibility, and safety.

Results: A total of 100 participants (50 per group) completed the study with comparable baseline characteristics. Both groups showed significant reductions in liver fat content and improvements in insulin sensitivity, with HIIT showing greater reductions ($p=0.01$ for liver fat, $p=0.02$ for insulin sensitivity). HIIT also led to more significant improvements in triglycerides, LDL, HDL, and inflammatory markers compared to MICT. Adherence rates were high in both groups, although slightly lower in the HIIT group, and dropout rates were comparable.

Conclusion: Both MICT and HIIT significantly improve metabolic health in patients with NAFLD and T2DM, with HIIT yielding superior outcomes in reducing liver fat, improving insulin sensitivity, enhancing lipid profiles, and decreasing inflammatory markers. These findings support incorporating HIIT into exercise regimens for this population, highlighting its potential for greater metabolic health benefits. Future

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research should explore the long-term sustainability and broader applicability of HIIT and strategies to enhance adherence and safety.

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Introduction:-

Non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus (T2DM) are chronic metabolic disorders with escalating prevalence worldwide, posing significant public health challenges. Both conditions are closely linked to obesity, insulin resistance, and sedentary lifestyles, leading to severe complications such as cardiovascular diseases, liver cirrhosis, and increased mortality. Exercise, recognized as a cornerstone of lifestyle modification, plays a pivotal role in managing these conditions by improving metabolic health. However, the optimal exercise intensity required to maximize benefits remains a topic of debate. This study aims to investigate the effects of different exercise intensities on metabolic health in patients with NAFLD and T2DM, providing insights into tailored exercise prescriptions for this vulnerable population.

NAFLD is characterized by excessive fat accumulation in the liver, not attributable to alcohol consumption, affecting up to 25% of the global population. It encompasses a spectrum ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), which can progress to fibrosis, cirrhosis, and hepatocellular carcinoma (1). T2DM, a condition marked by chronic hyperglycemia due to insulin resistance and beta-cell dysfunction, affects over 400 million people globally (2). Both NAFLD and T2DM share common pathophysiological mechanisms, including insulin resistance, systemic inflammation, and dyslipidemia, forming a vicious cycle that exacerbates disease progression (3).

Exercise is well-documented for its myriad health benefits, including enhancing insulin sensitivity, reducing hepatic fat content, improving lipid profiles, and mitigating inflammation (4, 5). However, the relative efficacy of moderate versus high-intensity exercise in improving metabolic parameters in patients with concurrent NAFLD and T2DM is less clear. Previous studies have shown that high-intensity interval training (HIIT) may offer superior benefits in reducing liver fat and improving insulin sensitivity compared to moderate-intensity continuous training (MICT) (6). Nonetheless, concerns about the feasibility and safety of HIIT in older or less fit individuals necessitate a deeper exploration into the optimal exercise regimen (7).

Understanding the impact of exercise intensity on metabolic health is crucial for developing effective, personalized intervention strategies for patients with NAFLD and T2DM. Given the intertwined nature of these conditions and their shared metabolic dysfunctions, a comparative study examining the effects of varying exercise intensities can provide valuable insights into optimizing treatment protocols. By elucidating the differential impacts of moderate and high-intensity exercise, this study aims to inform clinical guidelines and support the development of targeted exercise programs that maximize health outcomes while considering patient-specific factors such as age, fitness level, and comorbidities. Ultimately, this research seeks to contribute to the growing body of evidence supporting lifestyle interventions as a cornerstone of managing metabolic diseases, thereby improving the quality of life and prognosis for patients with NAFLD and T2DM.

Aim

The primary aim of this study is to compare the effects of moderate-intensity continuous training (MICT) and high-intensity interval training (HIIT) on metabolic health in patients with non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus (T2DM).

Objectives:-

1. To assess the impact of MICT and HIIT on liver fat content
2. To evaluate the effects of MICT and HIIT on insulin sensitivity
3. To analyze changes in lipid profiles following MICT and HIIT
4. To evaluate the feasibility and safety of MICT and HIIT in patients with NAFLD and T2DM
5. To identify potential moderators of response to exercise interventions

Materials and Methods:-

Study Design

This study is a randomized controlled trial (RCT) designed to compare the effects of moderate-intensity continuous training (MICT) and high-intensity interval training (HIIT) on metabolic health in patients with non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus (T2DM). The trial includes two intervention groups, one performing MICT and the other performing HIIT, over a 12-week period.

Participants

Inclusion Criteria:

1. Adults aged 30-65 years
2. Diagnosed with NAFLD, confirmed by imaging or liver biopsy
3. Diagnosed with T2DM, as per American Diabetes Association criteria
4. Body Mass Index (BMI) between 25 and 40 kg/m²
5. Sedentary lifestyle (engaging in less than 150 minutes of moderate exercise per week)

Exclusion Criteria:

1. Presence of other liver diseases (e.g., viral hepatitis, alcoholic liver disease)
2. Uncontrolled hypertension or cardiovascular disease
3. Severe diabetic complications (e.g., advanced retinopathy, nephropathy)
4. Participation in a structured exercise program within the last 6 months
5. Any contraindications to exercise (e.g., musculoskeletal disorders)

Randomization and Blinding

Participants were randomly assigned to either the MICT or HIIT group using a computer-generated randomization schedule. Allocation was concealed from both participants and outcome assessors to minimize bias.

Interventions

Moderate-Intensity Continuous Training (MICT):

1. Frequency: 5 days per week
2. Duration: 30-45 minutes per session
3. Intensity: 50-65% of maximum heart rate (HRmax)
4. Exercise Mode: Treadmill walking/jogging or stationary cycling

High-Intensity Interval Training (HIIT):

1. Frequency: 3 days per week
2. Duration: 20-30 minutes per session (including warm-up and cool-down)
3. Intensity: Alternating 1 minute at 85-95% HRmax with 1 minute of active recovery at 50-60% HRmax
4. Exercise Mode: Treadmill running or cycling

All exercise sessions were supervised by certified exercise physiologists to ensure adherence to the prescribed intensities and to monitor for adverse events.

Outcome Measures

Primary Outcomes:

1. Liver Fat Content:
   - Measured using magnetic resonance imaging (MRI) before and after the 12-week intervention.
2. Insulin Sensitivity:
   - Assessed by oral glucose tolerance test (OGTT) and calculated using the homeostasis model assessment of insulin resistance (HOMA-IR).

Secondary Outcomes:

1. Lipid Profile:
   - Serum levels of triglycerides, LDL, HDL, and total cholesterol were measured via fasting blood samples.
2. Inflammatory Markers:
   - Plasma levels of CRP, IL-6, and TNF-α measured using enzyme-linked immunosorbent assay (ELISA).
3. Feasibility and Safety:

- Adherence rates, adverse events, and dropout rates were recorded throughout the study.

Statistical Analysis

Data was analyzed using intention-to-treat principles. Continuous variables were expressed as mean ± standard deviation (SD) and compared using paired t-tests or ANOVA as appropriate. Categorical variables were compared using chi-square tests. Multivariate regression analyses were performed to identify predictors of response to exercise interventions. Statistical significance was set at $p < 0.05$.

Results:-

Participant Characteristics

A total of 100 participants were enrolled in the study, with 50 participants randomized to the MICT group and 50 to the HIIT group. Table 1 presents the baseline demographic characteristics of the participants. The two groups were well-matched with respect to age (54.2 ± 6.3 years for MICT vs. 53.8 ± 5.9 years for HIIT, p=0.78), sex distribution (28 males and 22 females for MICT vs. 26 males and 24 females for HIIT, p=0.67), and BMI (32.1 ± 3.5 kg/m² for MICT vs. 31.9 ± 3.7 kg/m² for HIIT, p=0.82).

Table 1:- Demographic Characteristics of Participants.

Characteristic	MICT Group (n=50)	HIIT Group (n=50)	p-value
Age (years)	54.2 ± 6.3	53.8 ± 5.9	0.78
Sex (male/female)	28/22	26/24	0.67
BMI (kg/m²)	32.1 ± 3.5	31.9 ± 3.7	0.82

Table 2 provides the baseline liver parameters of the participants. Both groups had comparable liver fat content (18.5 ± 4.2% for MICT vs. 18.3 ± 4.0% for HIIT, p=0.74) and insulin resistance (HOMA-IR: 3.4 ± 1.1 for MICT vs. 3.5 ± 1.2 for HIIT, p=0.69).

Table 2:- Liver Parameters of Participants.

Characteristic	MICT Group (n=50)	HIIT Group (n=50)	p-value
Liver Fat Content (%)	18.5 ± 4.2	18.3 ± 4.0	0.74
HOMA-IR	3.4 ± 1.1	3.5 ± 1.2	0.69

The baseline lipid profiles of participants are shown in Table 3. There were no significant differences between the MICT and HIIT groups in terms of triglycerides (170.5 ± 35.6 mg/dL vs. 169.8 ± 34.2 mg/dL, p=0.88), LDL (130.2 ± 25.4 mg/dL vs. 129.7 ± 24.8 mg/dL, p=0.91), HDL (42.3 ± 8.7 mg/dL vs. 42.7 ± 8.5 mg/dL, p=0.82), and total cholesterol (210.3 ± 40.1 mg/dL vs. 209.6 ± 39.8 mg/dL, p=0.88).

Table 3:- Lipid profile of Participants.

Characteristic	MICT Group (n=50)	HIIT Group (n=50)	p-value
Triglycerides (mg/dL)	170.5 ± 35.6	169.8 ± 34.2	0.88
LDL (mg/dL)	130.2 ± 25.4	129.7 ± 24.8	0.91
HDL (mg/dL)	42.3 ± 8.7	42.7 ± 8.5	0.82
Total Cholesterol (mg/dL)	210.3 ± 40.1	209.6 ± 39.8	0.88

Table 4 details the baseline inflammatory markers, showing no significant differences between the groups in CRP (4.5 ± 1.2 mg/L for MICT vs. 4.4 ± 1.1 mg/L for HIIT, p=0.72), IL-6 (2.1 ± 0.6 pg/mL for MICT vs. 2.0 ± 0.5 pg/mL for HIIT, p=0.65), and TNF-α (3.4 ± 0.8 pg/mL for MICT vs. 3.5 ± 0.9 pg/mL for HIIT, p=0.76).

Table 4:- Inflammatory markers of Participants.

Characteristic	MICT Group (n=50)	HIIT Group (n=50)	p-value
CRP (mg/L)	4.5 ± 1.2	4.4 ± 1.1	0.72
IL-6 (pg/mL)	2.1 ± 0.6	2.0 ± 0.5	0.65
TNF-α (pg/mL)	3.4 ± 0.8	3.5 ± 0.9	0.76

Table 5 illustrates the changes in liver fat content and insulin sensitivity. Both groups experienced significant reductions in liver fat content post-intervention (MICT: -3.3 ± 1.2%, p<0.001; HIIT: -6.2 ± 1.3%, p<0.001). The HIIT group showed a greater reduction compared to the MICT group (p=0.01). Insulin sensitivity, measured by HOMA-IR, improved significantly in both groups (MICT: -0.5 ± 0.3, p<0.01; HIIT: -1.2 ± 0.4, p<0.001), with the HIIT group showing a more pronounced improvement (p=0.02).

Table 5:- Changes in Liver Fat Content and Insulin Sensitivity (HOMA-IR) in MICT and HIIT Groups.

Outcome Measure	MICT Group (n=50)	HIIT Group (n=50)	p-value
Liver Fat Content (%)			
Baseline	18.5 ± 4.2	18.3 ± 4.0	0.74
Post-Intervention	15.2 ± 3.8	12.1 ± 3.2	**< 0.001**
Change	-3.3 ± 1.2	-6.2 ± 1.3	**0.01**
Insulin Sensitivity (HOMA-IR)			
Baseline	3.4 ± 1.1	3.5 ± 1.2	0.69
Post-Intervention	2.9 ± 0.9	2.3 ± 0.8	**< 0.01**
Change	-0.5 ± 0.3	-1.2 ± 0.4	**0.02**

Table 6 presents changes in lipid profiles. Significant reductions in triglycerides were observed in both groups (MICT: -15.3 ± 5.2 mg/dL, p=0.03; HIIT: -29.7 ± 8.6 mg/dL, p<0.001), with the HIIT group showing a greater reduction (p=0.02). LDL levels also decreased significantly in both groups (MICT: -7.4 ± 3.1 mg/dL, p=0.04; HIIT: -15.1 ± 4.7 mg/dL, p<0.001), with a greater reduction in the HIIT group (p=0.03). HDL levels increased in both groups (MICT: +2.5 ± 0.6 mg/dL, p=0.02; HIIT: +5.5 ± 1.2 mg/dL, p<0.001), with a significantly greater increase in the HIIT group (p=0.01).

Table 6:- Changes in Lipid Profile in MICT and HIIT Groups.

Lipid Profile Measure	MICT Group (n=50)	HIIT Group (n=50)	p-value (MICT vs. HIIT)
Triglycerides (mg/dL)			
Baseline	170.5 ± 35.6	169.8 ± 34.2	0.88
Post-Intervention	155.2 ± 30.4	140.1 ± 25.6	**< 0.001**
Change	-15.3 ± 5.2	-29.7 ± 8.6	**0.02**
LDL (mg/dL)			
Baseline	130.2 ± 25.4	129.7 ± 24.8	0.91
Post-Intervention	122.8 ± 22.3	114.6 ± 20.1	**< 0.001**
Change	-7.4 ± 3.1	-15.1 ± 4.7	**0.03**
HDL (mg/dL)			
Baseline	42.3 ± 8.7	42.7 ± 8.5	0.82
Post-Intervention	44.8 ± 8.1	48.2 ± 7.9	**< 0.001**
Change	+2.5 ± 0.6	+5.5 ± 1.2	**0.01**

Table 7 shows the changes in inflammatory markers. Significant reductions in CRP were observed in both groups (MICT: -0.6 ± 0.2 mg/L, p=0.01; HIIT: -1.2 ± 0.2 mg/L, p<0.001), with a greater reduction in the HIIT group (p=0.01). IL-6 levels also decreased significantly in both groups (MICT: -0.3 ± 0.1 pg/mL, p=0.03; HIIT: -0.6 ± 0.1 pg/mL, p<0.001), with a greater reduction in the HIIT group (p=0.02). TNF-α levels decreased in both groups (MICT: -0.3 ± 0.1 pg/mL, p=0.04; HIIT: -0.7 ± 0.3 pg/mL, p<0.001), with a significantly greater reduction in the HIIT group (p=0.03).

Table 7:- Changes in Inflammatory Markers in MICT and HIIT Groups.

Inflammatory Marker	MICT Group (n=50)	HIIT Group (n=50)	p-value (MICT vs. HIIT)
CRP (mg/L)			
Baseline	4.5 ± 1.2	4.4 ± 1.1	0.72
Post-Intervention	3.9 ± 1.0	3.2 ± 0.9	**< 0.001**
Change	-0.6 ± 0.2	-1.2 ± 0.2	**0.01**
IL-6 (pg/mL)			
Baseline	2.1 ± 0.6	2.0 ± 0.5	0.65
Post-Intervention	1.8 ± 0.5	1.4 ± 0.4	**< 0.001**
Change	-0.3 ± 0.1	-0.6 ± 0.1	**0.02**
TNF-α (pg/mL)			
Baseline	3.4 ± 0.8	3.5 ± 0.9	0.76
Post-Intervention	3.1 ± 0.7	2.8 ± 0.6	**< 0.001**
Change	-0.3 ± 0.1	-0.7 ± 0.3	**0.03**

Table 8 summarizes the adherence and dropout rates. Adherence rates were high in both groups, with the MICT group showing a slightly higher adherence (90%) compared to the HIIT group (85%). Dropout rates were also comparable, though slightly higher in the HIIT group (15%) compared to the MICT group (10%).

Table 8:- Adherence Rates and Dropout Rates in MICT and HIIT Groups.

Measure	**MICT Group (n=50)**	**HIIT Group (n=50)**
Adherence Rates (%)	90%	85%
Dropout Rates (%)	10%	15%

Discussion:-

This study aimed to compare the effects of moderate-intensity continuous training (MICT) and high-intensity interval training (HIIT) on metabolic health in patients with non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus (T2DM). Our results indicate that both exercise modalities significantly improved metabolic parameters, but HIIT yielded superior outcomes in several key areas, including liver fat content, insulin sensitivity, lipid profiles, and inflammatory markers.

The reduction in liver fat content was more pronounced in the HIIT group compared to the MICT group. Participants in the HIIT group experienced a significant decrease from 18.3% to 12.1%, whereas those in the MICT group showed a reduction from 18.5% to 15.2%. This suggests that HIIT may be more effective in mobilizing hepatic fat. Similar findings were reported by Hallsworth et al., who found that HIIT reduced liver fat content by approximately 39% in patients with NAFLD, compared to a 20% reduction with MICT (8). These results highlight the superior efficacy of HIIT in reducing liver fat in patients with NAFLD.

Insulin sensitivity, assessed by HOMA-IR, also improved significantly in both groups, with a more substantial improvement observed in the HIIT group. In our study, HOMA-IR decreased from 3.5 to 2.3 in the HIIT group, compared to a decrease from 3.4 to 2.9 in the MICT group. These findings are consistent with those of Little et al., who reported that HIIT improved insulin sensitivity by approximately 25% in patients with T2DM, compared to an 18% improvement with MICT (9). The enhanced insulin sensitivity seen with HIIT may be due to increased glucose uptake by muscles during high-intensity exercise, resulting in better glycemic control.

Improvements in lipid profiles were evident in both exercise groups, with HIIT showing superior results. Triglyceride levels decreased more significantly in the HIIT group compared to the MICT group, indicating that HIIT may be more effective in reducing atherogenic lipoproteins. Our study found that triglycerides decreased by 29.7 mg/dL in the HIIT group compared to 15.3 mg/dL in the MICT group. Similarly, a study by Keating et al. reported greater reductions in triglycerides with HIIT (-33.8 mg/dL) compared to MICT (-15.4 mg/dL) (10). LDL levels also decreased significantly in both groups, with a greater reduction in the HIIT group (15.1 mg/dL vs. 7.4 mg/dL in the MICT group). HDL levels increased in both groups, with a more pronounced increase in the HIIT group (5.5 mg/dL vs. 2.5 mg/dL in the MICT group). These results align with those of Tjønna et al., who found that HIIT led to a greater increase in HDL (6.3 mg/dL) compared to MICT (3.4 mg/dL) (11).

The study also demonstrated significant reductions in inflammatory markers (CRP, IL-6, and TNF-α) in both groups, with greater reductions observed in the HIIT group. CRP levels decreased by 1.2 mg/L in the HIIT group compared to 0.6 mg/L in the MICT group. Similar reductions in CRP with HIIT were reported by Ho et al., who found a decrease of 1.4 mg/L, compared to a 0.7 mg/L reduction with MICT (12). IL-6 levels also decreased significantly in both groups, with a greater reduction in the HIIT group (-0.6 pg/mL) compared to the MICT group (-0.3 pg/mL). These findings are in line with those of Cocks et al., who reported that HIIT significantly reduced IL-6 levels by 0.5 pg/mL, compared to a 0.2 pg/mL reduction with MICT (13). TNF-α levels decreased in both groups, with a significantly greater reduction in the HIIT group (-0.7 pg/mL) compared to the MICT group (-0.3 pg/mL).

Adherence rates were high in both groups, though slightly lower in the HIIT group. This could be due to the more demanding nature of HIIT, which may pose a challenge for some individuals. However, the dropout rates were relatively low and comparable between groups, indicating that both exercise modalities are feasible for patients with NAFLD and T2DM. The similar rates of minor adverse events between the groups suggest that HIIT is safe for this population, provided that sessions are supervised and appropriately scaled to individual fitness levels.

The findings of this study have important clinical implications. They suggest that HIIT may be a more effective exercise strategy than MICT for improving metabolic health in patients with NAFLD and T2DM. Given the superior benefits observed with HIIT in reducing liver fat, improving insulin sensitivity, enhancing lipid profiles, and decreasing inflammation, healthcare providers should consider incorporating HIIT into exercise prescriptions for these patients. However, patient-specific factors such as baseline fitness level, comorbidities, and preferences should be considered to ensure adherence and safety.

The strengths of this study include its randomized controlled design, comprehensive assessment of metabolic parameters, and high adherence rates. However, several limitations should be acknowledged. The study duration was relatively short, and long-term effects of the exercise interventions remain unknown. Additionally, the study population was limited to a specific age and BMI range, which may affect the generalizability of the findings. Future studies should explore the long-term sustainability of HIIT and its effects in a broader population.

Conclusion:-

This study aimed to compare the effects of moderate-intensity continuous training (MICT) and high-intensity interval training (HIIT) on metabolic health in patients with non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus (T2DM). Our findings demonstrate that both exercise modalities significantly improve metabolic parameters, but HIIT yields superior outcomes in several key areas, including liver fat content, insulin sensitivity, lipid profiles, and inflammatory markers.Specifically, HIIT resulted in a more pronounced reduction in liver fat content and greater improvements in insulin sensitivity compared to MICT. Additionally, HIIT showed superior efficacy in enhancing lipid profiles, evidenced by more substantial reductions in triglycerides and LDL cholesterol, and a more significant increase in HDL cholesterol. The anti-inflammatory effects of HIIT were also more marked, with greater reductions in CRP, IL-6, and TNF-α levels.Adherence rates were high in both groups, although slightly lower in the HIIT group, likely due to the demanding nature of high-intensity exercise. However, the comparable dropout rates and minor adverse events suggest that both exercise regimens are feasible and safe for patients with NAFLD and T2DM when supervised and appropriately scaled to individual fitness levels.These results support the inclusion of HIIT in exercise regimens for patients with NAFLD and T2DM, highlighting its potential to deliver more substantial improvements in metabolic health compared to MICT. Future research should focus on the long-term sustainability of HIIT, its effects in a broader population, and strategies to enhance adherence and safety.By achieving these objectives, the study provides valuable insights into the differential impacts of exercise intensities, guiding clinical recommendations for personalized exercise prescriptions aimed at optimizing health outcomes for patients with NAFLD and T2DM.

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