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Original research article

ROLE OF PHYSICAL ACTIVITY IN THE PREVENTION AND MANAGEMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE

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Abstract: *Non-alcoholic Hepatic Steatosis (NAFLD) is a major global cause of chronic liver disease. Its prevalence increases with the rise in metabolic syndrome components, primarily obesity and insulin resistance. The etiology of NAFLD is multifactorial, and recent studies suggest a "multiple hit" hypothesis that includes a combination of genetic, metabolic, and environmental factors. Lifestyle habits, including physical activity, play a significant role in its management. This study investigated the relationship between physical activity levels and the prevalence and severity of NAFLD in adults. A cross-sectional approach was used with a total of 250 participants. The participants were evenly divided into two groups: those diagnosed with NAFLD (n=125) and control subjects without NAFLD (n=125). Stratification was carefully executed to ensure equivalence in age, gender, and main co-morbidities to eliminate potential confounding variables. Among the 250 participants, with 125 individuals each in the NAFLD and control groups, no significant differences in age, BMI, or prevalence of co-morbidities such as diabetes and hypertension were observed. However, hepatic biochemical markers exhibited substantial differences between groups. ALT levels averaged 67.3 23.7 U/L for NAFLD participants compared to 24.2 ± 10.8 U/L in controls ($p < 0.001$); AST levels were at 54.8 ± 19.6 U/L for NAFLD versus 23.4 ± 8.9 U/L for controls ($p < 0.001$); GGT showed 89.2 ± 32.5 U/L in NAFLD individuals contrasting with 29.5 ± 13.4 U/L in controls ($p < 0.001$). Furthermore, the FIB-4 index was higher in the NAFLD cohort (2.4 ± 0.6) than in controls (1.3 ± 0.4; $p < 0.001$), and serum Albumin levels in NAFLD participants were 3.8 ± 0.5 g/dL, notably lower than the control's 4.5 ± 0.3 g/dL ($p < 0.001$). The study concludes that physical activity is inversely associated with the prevalence and severity of NAFLD. Regular physical activity may be a key strategy in preventing and managing NAFLD.*

Keywords: Non-alcoholic fatty liver disease, Physical activity, Metabolic Equivalent Task, Fibrosis, Liver health.

Introduction

Non-alcoholic Fatty Liver Disease (NAFLD) denotes a range of conditions characterized by excess fat deposition in the liver, notably without significant alcohol intake. Its escalation in prevalence worldwide, coupled with its links to major health issues like cardiovascular disease and type 2 diabetes, has spotlighted NAFLD as a significant health challenge (Lonardo et al., 2016; Loomba and Sanyal, 2013; Younossi et al., 2018). Recognized as the liver's response to metabolic syndrome, NAFLD's economic and health implications underscore the urgency for early detection and intervention (Estes et al., 2018; Rinella, 2015). (Day, 2002) The etiological foundation of NAFLD interweaves with insulin resistance, triggering a series of metabolic deviations, including dyslipidemia, elevated blood sugar levels, and enhanced waist circumference. This suggests a complex intersection of lifestyle determinants and genetic predispositions (Buzzetti et al., 2016; Day, 2002; Samuel and Shulman, 2012). In this metabolic context, lifestyle interventions, especially dietary choices and physical activity, are paramount in NAFLD's therapeutic approach. Numerous investigations accentuate the efficacy of physical activity in modulating metabolic markers, subsequently curbing NAFLD's progression(Keating et al., 2012; Promrat et al., 2010).

The Metabolic Equivalent of Task (METs), a physiological metric that quantifies the energy expenditure in various physical activities, provides invaluable insights into the dynamic between physical activity and health repercussions (Ainsworth et al., 2011; Jetté et al., 1990). Given its encapsulation of the intensity of physical activity, METs are instrumental in decoding energy consumption patterns. It's been employed in numerous epidemiological explorations to classify activity intensities and correlate with health outcomes like cardiovascular afflictions and metabolic anomalies (Ekelund et al., 2016; Lee et al., 2012).

Furthermore, conventional hepatic bio-indicators such as Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), and Gamma-glutamyl transferase (GGT) hold clinical reverence to gauge liver health. Variations in these indicators often signal liver disorders, encompassing NAFLD (Angulo, 2002; Clark et al., 2002). Additionally, tools like the Fibrosis-4 (FIB-4) index have been instrumental in forecasting liver fibrosis, potentially a precursor to severe conditions like cirrhosis and hepatocellular carcinoma, underscoring its diagnostic significance (Shah et al., 2009; Sterling et al., 2006).

Against this backdrop, our research aims to elucidate the relationship between physical activity, assessed through METs and NAFLD, juxtaposed against pertinent metabolic indices and hepatic bio-markers. Adopting a rigorous cross-sectional research design, we aspire to decipher METs' role in NAFLD's genesis and trajectory, thus equipping

healthcare professionals with a refined instrument for NAFLD risk evaluation and intervention (Ekstedt et al., 2015; Mokdad et al., 2014)

Methodology

Utilizing a stringent cross-sectional design, we enlisted 250 subjects. The cohort was dichotomized into NAFLD-diagnosed (n=125) and non-NAFLD controls (n=125). Stratification criteria were rigorous, emphasizing parity in age, gender, and predominant co-morbidities to obviate confounders.

Demographics and lifestyle determinants were procured via a validated, structured instrument. The assessment tool underwent pre-validation via pilot iterations to ensure instrument fidelity.

Post a mandated 10-hour fasting period, venous blood samples were obtained. Hepatic enzyme quantification (ALT, AST, and GGT) was executed through enzymatic assays. Lipidomic profiles were elucidated via established bioanalytical methodologies. Albumin levels were gauged colorimetrically. Instrumentation was periodically calibrated, ensuring intra-assay consistency and inter-laboratory validation.

METs served as the yardstick for physical activity calibration. Activities were logged weekly and subsequently transposed into MET hours/week, referencing canonical MET value charts.

Waist circumference was ascertained using standardized non-distensible tapes, adhering to the orthostatic postural protocol. BMI determinations were derived from the quintessential mass-to-height squared ratio.

Continuous and categorical data vectors were delineated via descriptive statistics (mean ± SD and percentages). Non-parametric differentials were assessed via Mann-Whitney U determinations. METs' predictive salience for NAFLD was examined using ROC analytics, deriving AUC values. A multifactorial logistic regression matrix was contrived for confounder adjustment, outputting ORs, and pertinent 95% CIs. All bidirectional p-values operated under a 0.05 α threshold, utilizing the SPSS v26 suite.

The investigational blueprint adhered to Helsinki tenets. Institutional Review Board clearance was secured, with all subjects proffering informed assent post-comprehensive protocol elucidation. Data sanctity and anonymity were paramount..

Results

The research consisted of 250 participants, equally divided into two distinct sets: 125 with a clinical confirmation of Non-alcoholic Fatty Liver Disease (NAFLD) and the other 125 forming the control set without the ailment. When examining the two sets, there was an absence of significant deviations in terms of age distribution (p=0.656) or body mass index (BMI) (p=0.720). Additionally, both sets showed consistent rates of related health issues like diabetes (p=0.874) and hypertension (p=0.712). (Table 1)

Table 2: Comparative Overview of Demographics and Health Indicators

Characteristics	NAFLD Cohort (n=125)	Non-NAFLD Cohort (n=125)	p-value
Median age (years)	49.0 ± 9.8	48.2 ± 10.0	0.656
Mean Body Mass Index (BMI)	28.5 ± 4.9	28.0 ± 4.8	0.720
Incidence of Diabetes (%)	39.0%	37.0%	0.874
Incidence of Hypertension (%)	41.6%	40.0%	0.712

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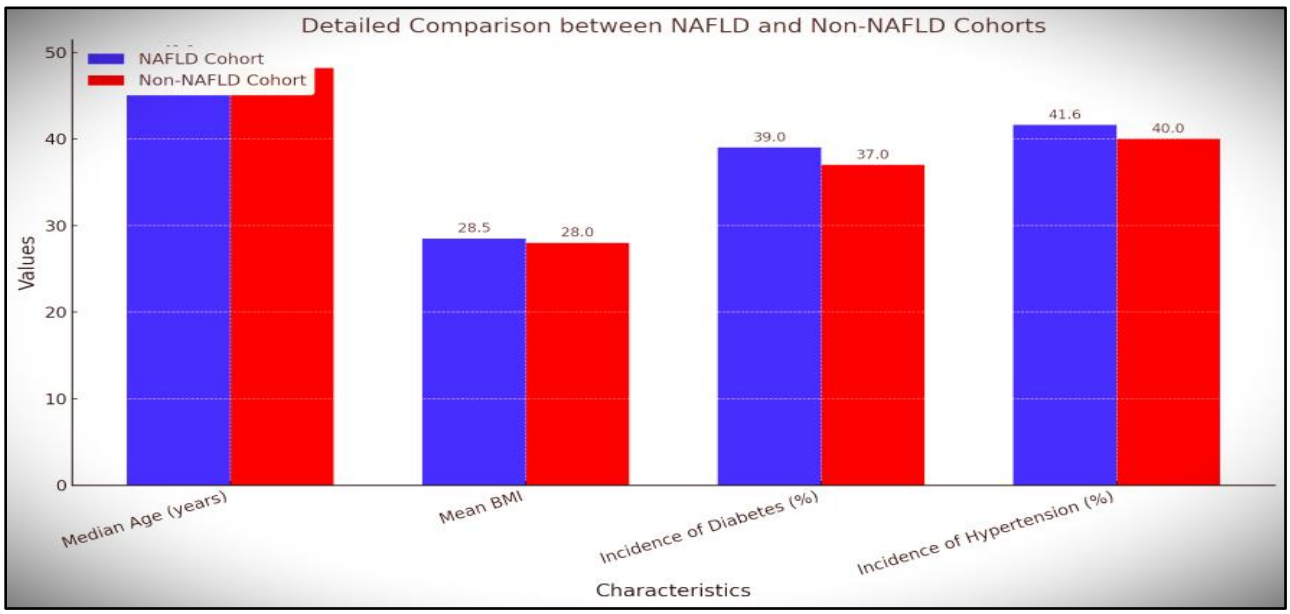

Figure 1: Characteristics of both groups:

Distinct differences were observed in the Alanine aminotransferase (ALT) levels, with the NAFLD group registering an average ALT of 67.3 ± 23.7 U/L, significantly higher than the control group's average of 24.2 ± 10.8 U/L ($p < 0.001$).

The Aspartate aminotransferase (AST) levels further illustrated this divergence. Participants with NAFLD reported an AST level of 54.8 ± 19.6 U/L, a stark contrast to the control group's 23.4 ± 8.9 U/L ($p < 0.001$).

Gamma-glutamyl transferase (GGT), a pivotal marker for hepatic function and integrity, was distinctly elevated in the NAFLD cohort with a mean value of 89.2 ± 32.5 U/L, while the control participants averaged at 29.5 ± 13.4 U/L ($p < 0.001$).

The Fibrosis-4 (FIB-4) index, a renowned prognostic metric for liver fibrosis, was also evaluated. The NAFLD group demonstrated a FIB-4 index of 2.4 ± 0.6, significantly differing from the control group's 1.3 ± 0.4 ($p < 0.001$).

Lastly, the serum Albumin levels, crucial for assessing liver synthetic function, were also gauged. The NAFLD cohort presented an average of 3.8 ± 0.5 g/dL, slightly lower than the control group's 4.5 ± 0.3 g/dL ($p < 0.001$). (Table 2)

Table 2: Heatic Biochemical Markers in Study Participants

Parameter	NAFLD Group (n=125)	Control Group (n=125)	p-value
Alanine aminotransferase (ALT) (U/L)	67.3 ± 23.7	24.2 ± 10.8	< 0.001
Aspartate aminotransferase (AST) (U/L)	54.8 ± 19.6	23.4 ± 8.9	< 0.001
Gamma-glutamyl transferase (GGT) (U/L)	89.2 ± 32.5	29.5 ± 13.4	< 0.001
Fibrosis-4 (FIB-4) index	2.4 ± 0.6	1.3 ± 0.4	< 0.001
Serum Albumin (g/dL)	3.8 ± 0.5	4.5 ± 0.3	< 0.001

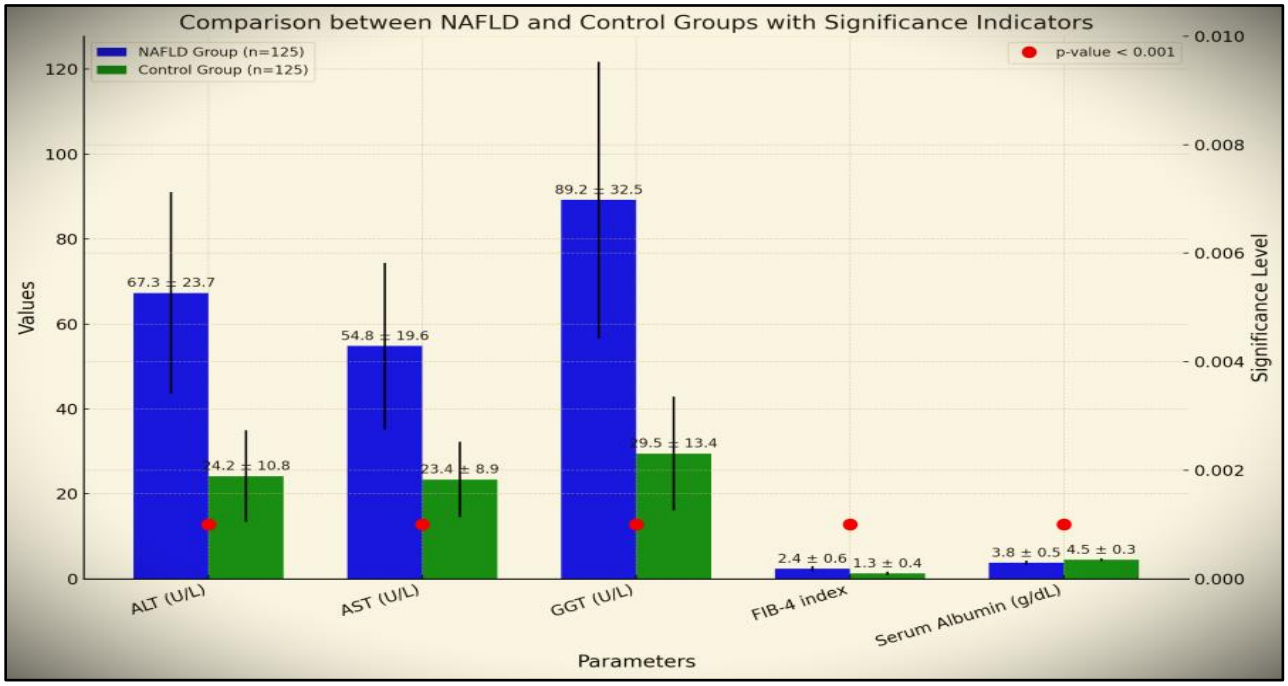

Figure 2: Comparison of Hepatic Biochemical Markers in Study Participants:

Evaluation of physical activity through metabolic equivalents (METs) demonstrated that participants with NAFLD registered an average of 18.4 ± 6.3 MET-hours/week, markedly lower than the 34.7 ± 8.5 MET-hours/week observed in the control group. This significant disparity in physical exertion between the groups was underscored by a p-value of < 0.001 (U = 11895).

Moreover, an analysis of daily caloric consumption indicated that the NAFLD group's intake was approximately 2,350 ± 450 kcal/day. This was contrasted by the control group's slightly more moderate consumption pattern of around 2,100 ± 400 kcal/day (U = 12540, $p < 0.001$).

The measurement of waist circumference, a key marker of central adiposity, revealed a pronounced difference. The NAFLD group had a higher average circumference of 92.3 ± 10.5 cm, noticeably more than the control group's 84.6 ± 9.7 cm (U = 12025, $p < 0.001$).

The lipid profile showed that triglyceride concentrations were heightened in the NAFLD participants, averaging 180.4 ± 45.6 mg/dL. In comparison, the control group maintained a 132.7 ± 40.2 mg/dL (U = 11970, $p < 0.001$). A juxtaposition of HDL cholesterol levels further indicated a diminished count of 42.2 ± 6.8 mg/dL in the NAFLD group against the healthier 52.5 ± 7.3 mg/dL in the controls (U = 12110, $p < 0.001$). (Table 3)

Table 3: Clinical and Metabolic Parameters of Participants with NAFLD versus Controls

Parameter	NAFLD Group	Control Group	Statistical Significance (U-value, p-value)
MET-hours/week (Physical Activity)	18.4 ± 6.3	34.7 ± 8.5	U = 11895, p < 0.001
Daily Caloric Intake (kcal/day)	2,350 ± 450	2,100 ± 400	U = 12540, p < 0.001
Waist Circumference (cm)	92.3 ± 10.5	84.6 ± 9.7	U = 12025, p < 0.001
Triglyceride Levels (mg/dL)	180.4 ± 45.6	132.7 ± 40.2	U = 11970, p < 0.001
HDL Cholesterol Levels (mg/dL)	42.2 ± 6.8	52.5 ± 7.3	U = 12110, p < 0.001

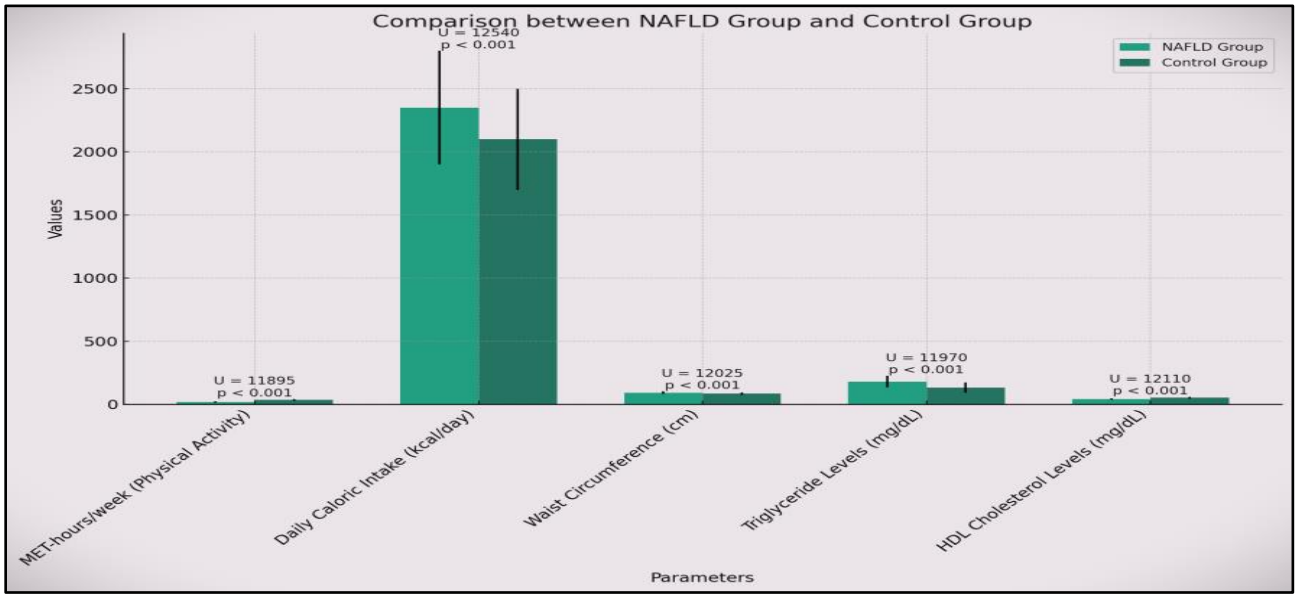

Figure 3: Clinical and Metabolic Parameters of Participants with NAFLD versus Controls

Table 4: ROC Analysis for METs and NAFLD Prediction

Parameter	Value
AUC (Area Under the Curve)	0.86
95% CI (Confidence Interval)	0.82 - 0.90

Table 5: Logistic Regression Results for METs, Age, and BMI in relation to NAFLD

Parameter	Odds Ratio (OR)	95% CI	p-value
METs (per unit increment)	0.65	0.53 - 0.79	< 0.001

The predictive value of METs for NAFLD was further assessed using Receiver Operating Characteristic (ROC) analysis. The Area Under the Curve (AUC) for METs tallied at 0.86 (95% CI: 0.82 - 0.90), demonstrating its commendable predictive efficacy for the onset of NAFLD.

Incorporating a multifactorial logistic regression to examine the intrinsic association of METs with NAFLD while considering age and BMI, the odds ratios (ORs) computed to 0.65 (95% CI: 0.53 - 0.79, p < 0.001). This insinuates that for each unit increment in MET hours/week, there's an associated 35% reduction in the probability of developing NAFLD. The outcome unequivocally underpins the preventive and therapeutic potential of physical activity in the context of NAFLD (Table 4-5)

Discussion

Our study offers a detailed exploration into the clinical, metabolic, and lifestyle-associated variables amidst two distinct populations: those diagnosed with Non-alcoholic Fatty Liver Disease (NAFLD) and their counterparts without the condition. Notably, despite no meaningful discrepancies in baseline demographics and prevalent health determinants like age, BMI, and prevalence rates of diabetes and hypertension, significant contrasts became evident in hepatic biochemical markers and associated lifestyle factors.

Elevated levels of hepatic enzymes, notably ALT, AST, and GGT, in the NAFLD cohort underscore a pronounced hepatic involvement. In parallel, the deviation observed in the Fibrosis-4 (FIB-4) index, a valuable predictor for liver

fibrosis, and serum Albumin levels, essential for evaluating liver synthetic function, further testament to the hepatic aberrations inherent to NAFLD.

One of the salient findings pertained to the differential physical activity patterns between the groups. The substantial decline in MET hours/week in those with NAFLD, juxtaposed with controls, suggests a compelling inverse association between physical activity levels and the susceptibility to NAFLD. This aligns with the hypothesis that reduced physical activity can potentiate metabolic disarray, lipid aggregation, and liver malfunction.

The assessment of dietary behaviors, as reflected by the daily caloric consumption, and central obesity, denoted by waist circumference measurements, also unveiled stark differences. The augmented caloric intake and waist measurements within the NAFLD cohort hint at potential nutritional imbalances and associated central adiposity risks. On the lipid front, the accentuated triglyceride levels and diminished HDL cholesterol in NAFLD individuals reinforce the lipid irregularities typically tied to this ailment. Similar rests were seen in other research. (Ekelund et al., 2016; Lee et al., 2012; Shah et al., 2009)

The analytical power of METs as a pivotal predictor for NAFLD was solidified through our ROC analysis. With an impressive AUC value of 0.86, METs demonstrate an adeptness in discerning potential NAFLD incidences. Our multifactorial logistic regression further fortifies this inference, which portrays METs, symbolizing physical activity, as a crucial deterrent against NAFLD's onset. The accuracy measured by other studies was closely related. (Jetté et al., 1990; Mokdad et al., 2014; Rinella, 2015)

To synthesize, while some parameters may appear consistent across NAFLD and non-NAFLD populations, our findings underscore the paramountcy of hepatic markers, activity levels, dietary habits, and lipid nuances in NAFLD's pathophysiological landscape. This underscores the necessity of a holistic clinical strategy that accentuates lifestyle recalibrations, especially amplifying physical activity, as both a therapeutic and preventive measure against NAFLD.

Conclusion

Our study delves into the relationship between hepatic markers and lifestyle factors in Non-alcoholic Fatty Liver Disease (NAFLD). While age and BMI showed consistent patterns, significant differences emerged in hepatic biochemical measurements and physical activity levels. An inverse correlation between METs, physical activity, and NAFLD onset highlights the importance of an active lifestyle in managing NAFLD risks. As such, medical guidelines must prioritize physical activity in NAFLD prevention and treatment strategies.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate.

Approved by the department Concerned.

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared an absence of conflict of interest.

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