Original Research Paper

Volume-8 | Issue-1 | January-2018 | PRINT ISSN - 2249-555X

Medicine

LOW AND MODERATE LEVEL OF PHYSICAL ACTIVITY IS A RISK FACTOR FOR NAFLD

Swapna Chaturvedi*	Phd Scholar, Department Of Food And Nutrition, Lady Irwin College, University Of Delhi, India. *Corresponding Author
Neena Bhatia	Associate Professor & Head, Department Of Food And Nutrition, Lady Irwin College, University Of Delhi, India.
Naval K Vikram	Professor, Metabolic Research Group, Department Of Medicine, All India Institute Of Medical Sciences, New Delhi, India.
RM Pandey	Professor & Head Department of Biostatistics , All India Institute Of Medical Sciences, New Delhi, India.
KS Madhusudan	Associate Professor, Department Of Radiodiagnosis, All India Institute of Medical Sciences, New Delhi, India.

ABSTRACT Nonalcoholic fatty liver disease (NAFLD) is a lifestyle disease. Lack of physical activity can worsen clinical condition of NAFLD patients.

Objectives: To assess Physical activity (PA) levels (low, medium and high) among individuals with NAFLD and without NAFLD and to study relationship of PA with NAFLD.

Methods: Case Control study with Ultrasound diagnosed NAFLD cases (n=160) and subjects without NAFLD (n=160) was conducted .The PA levels were studied using GPAQ, Version 2 , based on frequency and duration in work, travel and leisure domains.

Results: NAFLD cases had significantly higher values of waist and hip circumference and WHR ($p<0.05$). More than 50 % of NAFLD cases were physically inactive compared to Controls.($p<0.05$). Moderate level of PA, (OR 95% CI) ([2.6 (1.04-6.34), p=0.006)] and low PA ([6.0 (2.40-14.85), $p<0.001$)] were associated as a risk factor for NAFLD.

Conclusion: Low and Moderate level of Physical Activity is a risk factor for NAFLD.

KEYWORDS : NAFLD, Physical Activity, METS-minutes Score

Introduction:

Non-alcoholic fatty liver disease (NAFLD) has emerged as one of the most common chronic liver diseases globally. It is consequent to inappropriate eating habits and sedentary lifestyles. It includes a histological spectrum of diseases, such as nonalcoholic fatty liver (NAFL), non-alcoholic steatohepatitis (NASH), advanced fibrosis, cirrhosis and hepatocellular carcinoma.(1) The estimated prevalence rate of NAFLD may range from 5% to 40% in Asian countries.(2)

NAFLD patients are at higher risk of cardiovascular and liver related mortality. (3-4) Exercise is an important non pharmocological modality to prevent NAFLD and can attribute to improvement of patients physical fitness.(5)

Low amount and low intensity of physical activity is presented in NAFLD subjects compared to age matched controls.(6).There is also an emerging trend of increased periods of sedentary activities, which may be a risk factor for cardiac health and overall mortality, however the association with NAFLD per se has been scarcely reported.(7,8).

Aims and Objectives:

To study the Physical activity level (low, medium, high) among individuals with NAFLD and without NAFLD and to study the relationship of PA with NAFLD..

Materials and Methods:

Study Population-A hospital based , Case Control study was carried out from September 2015 to September 2016. A total of 320 subjects(160 Cases and 160 Controls)were included in the study. Participants were recruited from the OPD of Gastroenterology & Medicine Department at AIIMS.

Sample size calculation was done using the formula for comparing two means (Mean1 ± SD1, Mean2 ± Sd2), with statistical power of 80% and level of significance as 5%. Using the surrogate of body fat percent sample size was calculated as 160 Cases and 160 Controls.(9-10).

Sampling technique- Adults of both sexes between the age 18 to 60 years who fulfilled the criteria for either or Cases or Controls were included.

Consent: Informed and written consent was taken from the participants.

Inclusion criteria for Cases - Ultrasound proven fatty liver with or without histological confirmation in the past one month; by questionnaire that on-going or recent (6months) alcohol consumption is <21 (210 gms) drinks on average per week in men and < 14 drinks (140 gms) on average per week in women. (11). Inclusion criteria for Controls –Apparently healthy Individuals who volunteered (attendants of patients coming to OPD) with similar age and BMI were included.

The **Exclusion criteria (**Cases and Controls)**-** History of chronic liver disease and no history of intake of drugs causing fatty liver(steroids, valproic acid, methotrexate, tetracycline and tomoxifen), OC's/ Corticosteroids); Established diagnosis of Type 2 DM, CVD, Inflammatory Bowel disease, presence of other liver diseases and severe end organ diseases, HIV infection, pregnancy and lactation; Positive test for the presence of HBsAg, (Hepatitis B Surface Antigen), anti-HCV (Antibody to Hepatitis C Virus) and anti HIV antibody; Ongoing or recent alcohol consumption > 21 drinks (210 gms) on average per week in men and > 14 drinks (140 gms) on average per week in women within the past 6 months or history of alcohol abuse; Use of weight loss medications or participation in weight loss programs & refusal to provide consent in the study.

Ethical Approval: The study was approved by the Lady Irwin College Ethics Committee and AIIMS Ethics Committee.

Demographic and Household Information was collected regarding age, family profile, Socio-economic assessment was based on the educational status, occupation and income of the patient as suggested by the modified Kuppuswamy socio-economic scale, using a pretested suitable questionnaire cum interview schedule .(12).

Clinical and radiological assessments-All participants completed a pretested suitable – questionnaire cum interview schedule on family history, past medical history, history of drug use during previous six months. Systolic and Diastolic blood pressures were measured twice on the same day after a gap of 5 minutes, using an electronic instrument (Model: Omron).The mean of the two readings was taken .The

presence of hypertension was defined as systolic blood pressure of over 140 mmHg or diastolic blood pressure of over 90 mm Hg.(13).Screening of NAFLD and Non NAFLD cases was done by Trans abdominal ultrasonography of liver was performed using a 1-5 MHz curvilinear transducer (iU22, Philips, Netherlands) at Radiology Department of AIIMS.(14)

Anthropometric measurements- Height: The height was recorded to the nearest 0.1 cm, using a stadiometer. Weight: Weight was recorded to the nearest 100g,using a digital scale (Model- Seca).Waist circumference was measured to the nearest 0.1 cm at the end of normal expiration. Hip circumference was recorded to the nearest 0.1 cm. The WC and HC were measured at the level midway between the lowest rib and the iliac crest and at the level of the great trochanter, respectively. Body Mass Index (BMI): BMI was calculated by Quetelet's ratio (Weight in kilograms divided by the square of height in meters). Cut offs of BMI and Waist - Hip Ratio, suggested for Asian Indian population were used.(15)

Physical Activity Assessment-Physical Activity Pattern was assessed using the Global Physical Activity Questionnaire (GPAQ) Version 2.(16) Information of physical activity was collected in 3 domains(activity at work, travel and recreational activities) along with information on sedentary behavior. Physical activity level was also categorized into low, moderate and high according to reported frequency and duration of physical activity.(16)*

Metabolic Equivalent values were applied to activity levels for calculation of total physical activity. The moderate intensity and vigorous intensity activities were assigned MET values of 4 and 6 respectively. The product of intensity (MET), frequency(per week) and duration(min) of each activity gave the total PA as denoted by MET minutes per week. Based on guidelines for Analysis of the GPAQ, Version 2,subjects were divided into 3 physical activity levels: Low PA category –if the value of MET score /week does not reach for either high or moderate level of PA. Moderate PA category –if the individual meets one of these criteria- 3 days or more, each day at least more than 60 minutes of vigorous PA or 5 days or more, each day atleast more than 150 minutes of moderate PA and travel or 5 days a week, any combination of moderate ,travel or vigorous activity, if the total score of PA reaches a minimum of 600 MET-min/week. High PA category-if the individual meets one of these criteria-doing at least 3 days of vigorous PA, which reaches the minimum of 1500 MET-min/week or 7 days a week, any combination of moderate ,travel or vigorous activity, if the total score of PA reaches a minimum of 3000 MET-min/week(16).

Statistical Analysis: Data was analysed by using statistical software STATA 14.0.Qualitative data expressed as frequency and percentage, quantitative data as Means ± SD and Median (Interquartile). Independent t test and Mann Whitney U test was used to compare the quantitative variable between the group. Logistic regression analysis was used to estimate Odds by adjusting confounding factors. ($p<0.05$) was considered as statistically significant.

RESULTS:

TABLE 1. Baseline Characteristics Of Cases And Controls

Variable	NAFLD Cases(n=160) Mean±SD n (%)	Controls (n=160) Mean±SD n (%)	p value
Age (Years)	39.8±8.4	39.4±8.6	0.699
BMI (kg/m)	26.9± 3.4	26.8 ± 3.6	0.809
Height (cms)	162.0± 8.6	159.56 ± 8.71	0.012
Weight(kg)	70.8±11.6	68.51± 11.5	0.068
Waist Circumference (cms)	86.57 ± 8.8	81.05 ±7.86	<0.001
Hip Circumference(cms)	100.53± 8.8	96.88 ±8.18	0.0002
WHR	0.86 ± 0.09	0.83± 0.78	0.003
Systolic BP(mm Hg)	127.03 ± 8.67	118.91± 5.89	<0.001
Diastolic BP(mm Hg)	81.49 ± 5.06	78.42± 5.51	<0.001
Pulse Rate	79.83 ± 5.45	73.08 ± 4.31	<0.00
Alcohol n(%)	33(20.63)	18(11.25)	0.022
Smoking n(%)	12(7.5)	19(11.88)	0.186

Table 1. shows the mean age of cases and controls was comparable i.e 39.8±8.4 years and 39.4 ±8.6 years respectively. The mean BMI of cases and controls was 26.9 ±3.4 and 26.8 ±3.6 respectively and was comparable. Patients with NAFLD had significantly higher values of waist and hip circumference, WHR, presence of hypertension and alcohol consumption ($p<0.005$).

Presence of hypertension (66% versus 7%),alcohol consumption (21% versus 11% ($p<0.05$),family history of overweight(18% versus 9%), T2DM(28% versus 17%),Metabolic Syndrome(30% versus 3%) ($p<0.05$) were all higher in cases versus controls respectively.

Physical Activity

In Cases versus controls low level of Physical activity was present in 55.62 % versus 31.8 % ($p= <0.001$),moderate level of PA in 39.37 % versus 52.5 % ($p= 0.040$),and high level of PA in 5.0% versus 15.62 % ($p= <0.001$).

Table 2-Median Mets –Minutes Score/Week And Median Minutes /Week For Various Domains Of Activity

Physical Activity Domain	NAFLD Cases(n=160) Median(IQR)	Controls(Without NAFLD(n=160) Median(IQR)	p value
Work Vigorous	360 (40-480)	560 (520-2160)	0.018
Work Vigorous Minutes /week	45 (7.5-60)	70 (70-180)	0.014
Work Moderate	520(380-980)	720 (480-1120)	0.382
Work Moderate Minutes /week	120 (100-210)	150 (120-210)	0.418
Travel	720 (400-840)	800 (600-1680)	0.005
Travel Minutes /week	180 (100-210)	210 (150-420)	0.004
Recreation Vigorous	1680 (600-4800)	1040(480-1440)	0.205
Minutes /week	210 (75-600)	130 (60-180)	0.205
Recreation Moderate	600 (540-2240)	360 (240-1440)	0.234
Minutes /week	150 (135-560)	90 (60-210)	0.190
Total Mets Score/week	720(420-1200)	1200(720-2720)	<0.001
Sedentry minutes/day	360(240-600)	300(240-480)	0.006

Table 2. shows the Median Mets –Minutes Score/week for Work domain of Vigorous Intensity and for Travel domain was higher in Controls compared to Cases and was statistically significant ($p<0.005$).

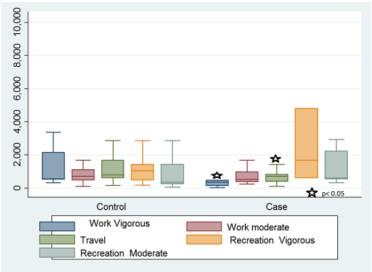
The Controls spent more time in Vigorous activity related to work (70 minutes/week) compared to NAFLD Cases(45 minutes/week) and the difference was statistically significant($p=0.014$)..

There was a statistically significant difference between the 2 groups in travel time (210 minutes/week in Controls versus 180 minutes/week in Cases; $p=0.004$).

The Median (IQR) Total MET score per week in Controls was 1200 (720-2720) per week, compared to 720 (420-1200) per week in NAFLD Cases ($p<0.001$),implying that NAFLD cases were physically inactive compared to their healthy counterparts.

The sedentary time was higher in NAFLD subjects (360 minutes per day versus Controls (300 minutes per day and statistically significant ($p<0.001$).

Figure 1. shows the Box and Whiskers plot for the Median (IQR)Mets -Minutes Score/week in NAFLD cases versus controls across 3 domains of Work, travel and recreation.



On logistic regression analysis, moderate level of PA, OR, 95% CI ([2.6 (1.04-6.34) , p=0.006)] and low PA ([6.0(2.40-14.85), p=<0.001)] were associated as a risk factor for NAFLD. On adjustment with age, gender, BMI and WHR, moderate PA ([2.6 (1.02-6.72), p=0.045)] and low level ([5.9 (2.23-15.30), p<0.001)] of PA still remained significant as a risk factor for NAFLD.

On adjustment with age, gender, BMI,WHR ,smoking ,alcohol and blood pressure the odds for moderate PA ([2.2 (0.81-5.77), p=0.120)] and low level of PA remained higher and significant as a risk factor for NAFLD(OR, 95% CI ([5.5 (2.04-14.97), p<0.001)]

Discussion:

The study data describes that low and moderate physical activity is a risk factor for NAFLD as compared to high level of physical activity .Studies have revealed that lower levels of physical activity and sedentary behavior is associated with NAFLD(6,17,18).

Training of Vigorous Intensity type can tackle hepatic steatosis with obesity and impaired glucose tolerance phenotype (19).Reduction in liver fat and improvement in cardiac function was reported by high-intensity interval training in NAFLD subjects. (20) The volume of Moderate to vigorous physical activity is an important factor for managing NAFLD.(21).

The study data showed that NAFLD patients spent more time in sedentary activity compared to healthy controls.(Mean of 6.75 hours±3.29hrs versus 5.74 hours± 2.76 hours; p< 0.001) .Other studies have also reported higher levels of sedentary behavior(22-23),which may predispose an adult to be at risk of becoming overweight or developing metabolic disorders

Considering the strong link between BMI and NAFLD, it is possible that main effect of physical activity on NAFLD is through its association with body weight. In our study also, on adjustment with BMI and WHR, low and moderate PA remained significant as a risk factor for NAFLD.

NAFLD was significantly associated with hypertension in our study. Hypertension was also reported to be associated with NAFLD in other studies.(24-27).Risk for NAFLD was significantly higher among participants who had a higher waist circumference This was similar to previous studies where significant associations of NAFLD with waist circumference have been reported.(25-28).

Conclusion- Our findings showed that low and moderate physical activity levels were significantly higher in Cases than Controls . Education of NAFLD patients on increasing their physical activity intensity may prevent disease progression and further complications and should be undertaken as part of the standard care procedures in a clinical setting. Future interventional studies are required to confirm our findings.

References :

1. Goh GB, McCullough AJ. Natural History of Nonalcoholic Fatty Liver Disease. Dig Dis Sci. 2016 May;61(5):1226-33.doi: 10.1007/s10620-016-4095-4. Epub 2016 Mar 22. PubMed PMID: 27003142.
2. Ray K. NAFLD-the next global epidemic. Nat Rev Gastroenterol Hepatol .Nat Rev Gastroenterol Hepatol. 2013 Nov;10(11):621. doi: 10.1038/nrgastro.2013.197. PubMed PMID: 24185985.
3. Anstee QM, Targher G, Day CP. Progression of NAFLD to diabetes mellitus, cardiovascular disease or cirrhosis. Nat Rev Gastroenterol Hepatol 2013; 10: 330-344 PubMed PMID: 23507799 DOI: 10.1038/nrgastro.2013.41 .
4. Gaggini M, Morelli M, Buzzigoli E, DeFronzo RA,Bugianesi E, Gastaldelli A. Non-alcoholic fatty liver disease (NAFLD) and its connection with insulin resistance, dyslipidemia, atherosclerosis and coronary heart disease. Nutrients 2013;5:1544-1560 PubMed PMID: 2366609 DOI: 10.3390/nu5051544.
5. Zelber-Sagi S, 2014. Effect of resistance training on non-alcoholic fatty-liver disease a randomized-clinical trial. World J Gastroenterol. 2014 Apr 21;20 (15):4382-92. doi: 10.3748/wjg.v20.i15.4382. PubMed PMID: 24764677. PubMed Central PMCID: PMC3989975.
6. Gerber L, Otgonsuren M, Mishra A, Escheik C, Birerdinc A, Stepanova M, Younossi ZM. Non-alcoholic fatty liver disease (NAFLD) is associated with low level of physical activity: a population-based study. Aliment Pharmacol Ther 2012; 36: 772-781 doi : 10.1111/apt.12038. PubMed PMID: 22958053 .
7. Wilmot EG, Edwardson CL, Achana FA, Davies MJ, Gorely T, Gray LJ, et al. Sedentary time in adults and the association with diabetes, cardiovascular disease and death: systematic review and meta-analysis. Diabetologia. 2012; 55: 2895–2905. PubMed PMID: 22890825.
8. Henson J, Yates T, Biddle SJ, Edwardson CL, Khunti K, Wilmot EG, et al. Associations of objectively measured sedentary behaviour and physical activity with markers of cardiometabolic health. Diabetologia. 2013;56:012–1020.PubMed PMID: 23456209 .
9. Nigam P, Bhatt SP, Misra A, Vaidya M, Dasgupta J, Chadha DS. Non-alcoholic fatty liver disease is closely associated with sub-clinical inflammation: a case-control study on Asian Indians in North India. PLoS One. 2013;8(1):e49286. doi: 10.1371/journal.pone.0049286. Epub 2013 Jan 11. PubMed PMID: 23326306. PubMed Central PMC ID: PMC3543427.
10. Thakur ML,Sharma S,Kumar A,Bhatt SP, Luthra K, Guleria R, Pandey RM, Vikram NK. Non alcoholic fatty liver disease is associated with subclinical atherosclerosis independent of obesity and metabolic syndrome in Asian Indians. Atherosclerosis. 2012 Aug; 223(2):507-11.doi: 10.1016/j.atherosclerosis.2012.06.005.Epub 2012 Jun 3. PubMed PMID: 22748277.
11. Chalasani N1, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K, Charlton M, Sanyal AJ; The diagnosis and management of non-alcoholic fatty liver disease: Practice guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association,2012.Jun;107(6):811-26. doi: 10.1038/ajg.2012.128. PubMed PMID: 22641309.
12. Gururaj & Maheshwaran . Kuppuswamy's Socio-Economic Status Scale – A Revision of Income Parameter For 2014. International Journal of Recent Trends in Science And Technology, ISSN 2277-2812 E-ISSN 2249-8109, Volume 11, Issue 1, 2014 pp 01-02 Copyright © 2014, Stat person Publications.
13. Armstrong C; Joint National Committee.JNC 8 Guidelines for the Management of Hypertension in Adults. Am Fam Physician. 2014 Oct 1; 90(7):503-504.PubMed PMID:25369633.
14. Bhat G, Baba CS ,Pandey A, Kumari N and Choudhuri G. Life style modification improves insulin resistance and liver histology in patients with non-alcoholic fatty liver disease. World J Hepatol. 2012 Jul 27; 4(7):209–217. doi:10.4254/ wjh.v4.i7.209.Pub Med Central PMC 3409355.
15. Misra A, Chowbey P, Makkar BM, Vikram NK, Wasir JS,Chadha D, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity,medical and surgical management. J Assoc Physicians India 2009;57:163-70.
16. World Health Organization. Global Physical Activity Questionnaire (GPAQ) Analysis Guide. Surveillance and Population-Based Prevention. Prevention of Noncommunicable Diseases Department. Geneva: World Health Organization; Available from:http://www.who.int/chp/steps/resources/GPAQ_Analysis_Guide.pdf.
17. Hallsworth K, Thoma C, Moore S, et al. Non-alcoholic fatty liver disease is associated with higher levels of objectively measured sedentary behavior and lower levels of physical activity than matched healthy controls. Frontline Gastroenterol 2015;6: 44
18. Long MT, Pedley A, Massaro J M et al. "Hepatic steatosis is associated with lower levels of physical activity measured via accelerometry," Obesity (Silver Spring). 2015 Jun;23(6):1259-66. doi: 10.1002/oby.21058. Epub 2015 May 9. PubMed PMID: 25959049 PubMed Central. PMCID:PMC4446168.
19. Cho J, Kim S, Lee S, Kang H. Effect of training intensity on nonalcoholic fatty liver disease. Med Sci Sports Exerc 2015;47(8):1624-34. doi: 10.1249/MSS. 0000000000000595. PubMed PMID: 25539480.
20. Hallsworth K, Thoma C, Hollingsworth KG, Cassidy S, Anstee QM, Day CP, et al. Modified high-intensity interval training reduces liver fat and improves cardiac function in non-alcoholic fatty liver disease: a randomized controlled trial. Clin Sci Lond 2015 Dec;129(12):1097105.doi:10.1042/CS20150308. Epub 2015 Aug 11.
21. Oh S, Shida T, Yamagishi K, Tanaka K, So R, Tsujimoto T, Shoda J,2015. Moderate to vigorous physical activity volume is an important factor for managing nonalcoholic fatty liver disease: a retrospective study. Hepatol Baltim Md 61, 1205–1215. doi:10.1002/hep.27544
22. Ryu S, Chang Y, Jung HS, Yun KE, Kwon MJ, Choi Y, Kim CW, Cho J, Suh BS, Cho YK, Chung EC, Shin H, Kim YS, 2015. Relationship of sitting time and physical activity with non-alcoholic fatty liver disease. J Hepatol. 2015 Nov;63(5):1229-37. doi: 0.1016/j.jhep.2015.07.010. Epub 2015 Sep 15. PubMed PMID: 26385766
23. Helajärvi H, Pahkala K, Heinonen OJ, et al. Television viewing and fatty liver in early midlife. The Cardiovascular Risk in Young Finns Study. Ann Med. 2015;47(6):519-26. doi: 10.3109/07853890.2015.1077989. Epub 2015 Sep 11. PubMed PMID: 26362414.
24. Sharda M, Yagnik D , Soni A and Nigam H.Non-alcoholic Fatty Liver Disease (NAFLD and its association with metabolic syndrome and cardiovascular diseases. International multispecialty Journal of Health (IMJH)[Vol-1,Issue-8,Oct.- 2015]
25. Singh SP, Singh A, Misra D, Misra B, Pati GK, Panigrahi MK, Kar SK, Bhuyan P, Pattnaik K, Meher C, Agrawal O, Rout N, Swain M, Aich P. Risk Factors Associated With Non-Alcoholic Fatty Liver Disease in Indians: A Case-Control Study. J Clin Exp Hepatol.2015. Dec; 5(4):295 302.doi:10.1016/j.jceh.2015.09.001. Epub 2015 Sep 8. PubMed PMID: 26900270. Pub Med Central PMCID: PMC4723647.9.
26. Bhatt SP, Misra A, Nigam P, Guleria R, and Pasha MA .Phenotype, Body Composition, and Prediction Equations (Indian Fatty Liver Index) for Non-Alcoholic Fatty Liver Disease in Non-Diabetic Asian Indians: A Case-Control Study. PubMed Central PMCID: PMC4657982.
27. Majumdar et al. Prevalence of NAFLD among adults in rural India. Indian J Public Health. 2016 Jan-Mar;60(1):26-33. doi: 10.4103/0019-557X.177295. PubMed PMID: 26911214.