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Original Article

Association of Level of Physical Activity, Diet and Lipid Profile with Non-alcoholic Fatty Liver Disease – A Case Control Study.

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Abstract

Background: Spectrum of liver pathology that develops in the absence of alcohol abuse or any other predisposing medical condition is being recognised as a major health issue, ranging from simple steatosis to florid cirrhosis and hepatocellular carcinoma. **Objectives:** To study the association between level of physical activity, dietary pattern and lipid profile in subjects diagnosed with NAFLD compared with controls. **Methods:** The study was conducted with 33 persons diagnosed with NAFLD and 31 controls in the department of physiology with the support of the Department of Radio diagnosis of Pushpagiri Institute of Medical Sciences and Research Centre. **Results:** The level of physical activity as measured by MET score in the NAFLD group was 948.80±628.4 (Mean±SD) and 4475.77±3202.3 (Mean ±SD) in the control group with a p value of < 0.001. 26 out of 31 participants in the control group (83.9%) were having high level of physical activity and only 4 out of 33(12.1%) had high level of physical activity in the NAFLD group. Low level of physical activity was reported by 15 out of 33 participants in the NAFLD group as compared to none in the control group. Moderate physical activity levels were reported by 14 out of 33 participants (42.4%) in the NAFLD group and 5 out of 31 participants 5(16.1%) in the control group and the difference is statistically significant (p<0.001). The calorie consumption in the NAFLD group was 2576.48±364.41 (Mean ± SD) and 2305.19±323.35 in the control group with a p value of 0.003. Both BMI and the waist hip ratio were found to be significantly greater in the NAFLD group compared to controls. But the p value was more for BMI (p=0.001 OR=6.8 CI=2.07–22.2) as compared to WHR (p=0.04 OR=2.77 CI =1.0007–7.6). SGPT levels was more in the NAFLD group (70.94±73.2) as compared to controls (37.71±32.5) with a p value of 0.001(OR=5.75 CI=1.948–16.968). **Conclusion:** Physical activity has a strong inverse relationship with Non-Alcoholic Fatty Liver Disease but excess calorie intake and obesity has vice versa relationship. The only biochemical abnormality found was an elevation in SGPT levels in the NAFLD group.

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Introduction

Non-alcoholic fatty liver disease (NAFLD) is a common condition characterised by excess hepatic lipid accumulation in the absence of significant amount of alcohol intake (>20 g per day) or any other medical conditions that are known to produce steatosis (1). This includes a spectrum that ranges from simple steatosis at the benign end to hepatocellular carcinoma (HCC) at the other end (2). Even though fatty liver disease does not progress to severe liver disease in most of the cases, on an average of 20% to 30% of patients will have histologic signs of fibrosis and necro-inflammation which indicates the presence of non-alcoholic steatohepatitis (NASH) (3, 4).

Many cases of cryptogenic cirrhosis are likely to be end stage NASH. Retrospective, case-control studies have shown that features suggestive of NASH are more frequent in Hepato Cellular Carcinoma (HCC) complicating cryptogenic cirrhosis than in matched HCC patients with known etiology (5-8). Like the western population, the incidence of metabolic syndrome and thus NAFLD is on the rise in our population. Prevalence of the disease is estimated to be around 9-32% in the general Indian population, with a higher incidence amongst obese and diabetic patients (9, 10).

The available data about physical activity among subjects affected with NAFLD suggest that the population participates in a low amount as well as low intensity of physical activity (11-13). Many studies have demonstrated the inverse relation between habitual physical activity and intrahepatic fat content (14).

It has been suggested in many studies that excess calories in the diet both in terms of total calories and the macronutrient composition has been implicated in the pathogenesis of NAFLD. The diet in NAFLD population revealed higher proportions of carbohydrates and fats (15, 16).

Body Mass Index (BMI) of 30 or more has also been associated with NAFLD. Truncal obesity even with a normal BMI seems to be an important risk factor for progression of NAFLD to NASH (17).

The elevations in and Serum Glutamic Oxaloacetic Transaminase (SGOT), Serum Glutamic Pyruvic Transaminase (SGPT) is the most common biochemical abnormality associated with NAFLD. But it is typically mild when present and are usually not greater than four times the upper limit of normal (15-17).

Our study proposes to find out the association of the level of physical activity, dietary habits, obesity, SGOT and SGPT levels along with serum lipid profile with NAFLD.

Methods

Ethics committee clearance was obtained from Pushpagiri Institute of Medical Sciences and Research Centre (Ref. No. PIMSRC/E1/388A/56/2013) dated 30/12/2013. Department of physiology and Radio-diagnosis, of Pushpagiri Institute of Medical Sciences and Research Centre jointly had taken up this study.

Study population

The cases and controls were selected from individuals attending regular health check-up in our institution.

Study design

A retrospective case control study design was taken to assess the potential risk factors associated with development of NAFLD from January 2014 to October 2015.

Definition of cases

The study was done in cases diagnosed with fatty liver by ultrasound in the radiology department of our hospital who does not have a daily alcohol consumption of > 20 g/day or a weekly consumption of > 140 g in the age group between 20-60 yrs. who are willing to participate and obtained informed consent from them.

Inclusion criteria

- All patients with NAFLD in the age group 20-60 yrs.
- No History of any other chronic liver disease

Exclusion criteria

- History of previous and / or present liver disease other than NAFLD.
- Long term drug therapy with drugs having proven hepatotoxicity.
- History of alcohol intake.

Definition of controls

Controls were randomly selected from individuals who does not have history of NAFLD attending the regular health check-up in our institution and who are willing to participate in the study by giving an informed consent and belong to the age group 20-60 yrs.

Methods of Assessment

Physical activity

The level of physical activity was measured by questionnaire method using the International Physical Activity Questionnaire (IPAQ). The IPAQ was developed by a group of experts in 1998 to facilitate surveillance of physical activity based on a global standard. We have used the last 7-day recall version of the IPAQ by direct interview of the participants. IPAQ assesses physical activity undertaken across a comprehensive set of domains including:

A. Leisure time physical activity

B. Domestic and gardening (yard) activities

C. Work-related physical activity

D. Transport-related physical activity

Both categorical and continuous indicators of physical activity are possible from both IPAQ forms. Data collected with IPAQ can be reported as a continuous measure. One measure of the volume of activity can be computed by weighting each type of activity by its energy requirements defined in METs to yield a score in MET–minutes. MET-minute scores are equivalent to kilocalories for a 60-kilogram person. Kilocalories may be computed from MET-minutes using the following equation: MET-min x (weight in kilograms/60 kilograms). MET-minutes/day or MET-minutes/week can be presented although the latter is more frequently used and is thus suggested. There are three categories of physical activity proposed to classify populations: High, Moderate and Low.

Diet

The dietary intake assessment was done with 24 hr dietary recall method which provides a representative dietary intake of the participants. Participants were asked to recall all the food items consumed on the previous day, total calorie intake and contribution from macronutrients were calculated and compared with recommended dietary allowances as calculated by the Harris Benedict formula.

Obesity

The Body Mass Index (BMI) and Waist Hip Ratio (WHR) was calculated according to the standard protocol and participants were classified accordingly.

Biochemical parameters

The biochemical parameters that were compared between the two groups were Fasting Blood Sugar (FBS), Serum Glutamic Oxaloacetic Transaminase (SGOT), Serum Glutamic Pyruvic Transaminase (SGPT), Alkaline phosphatase (ALP), Total Cholesterol, High Density Lipoproteins (HDL), Low Density Lipoproteins (HDL), Triglycerides and Total protein.

Statistical analysis

Statistical analysis was done with SPSS 17.0 software. All values are expressed as Mean±SD and compared by Pearson Chi square test except for dietary analysis for which Mann-Whitney test was

used. Odds ratios were calculated for the categorical variables comparing the cases and controls.

Results

33 Cases and 31 controls were selected for the study who satisfied the inclusion and exclusion criteria. The groups were well matched with respect to both age (p=0.67) and sex (p=0.45).

TABLE I: Subject characteristics.

Variable	*Cases (n=33)*	*Controls (n=31)*	*p (Significant <0.05)*
Age≠	42.42±8.99	44.09±10.93	0.45
Sex*			
Male	21 (66.6%)	16 (51.6%)	0.67
Female	12 (36.4%)	15 (48.4%)	
BMI≠	27.04±7.56	25.2±3.4	0.219
Waist hip ratio≠	0.94±0.07	0.95±0.1	0.542
FBS≠	105.09±24.8	96.39±26.04	0.176
SGOT≠	50.06±55.86	29.29±13.42	0.05
SGPT≠	70.94±73.2	37.71±32.5	0.024
ALP≠	199.27±45.3	195.23±59.3	0.759
Total cholesterol≠	202.18±38.5	199.77±37.5	0.801
HDL≠	42.06±9.6	49.45±11.5	0.46
LDL≠	127.18±28.8	120.93±33.06	0.423
Triglycerides≠	163.18±86.1	137.32±93.9	0.257
Total protein≠	7.18±0.42	6.95±1.3	0.327
MET score≠	948.80±628.4	4475.77±3202.3	<0.001
Physical activity*			
Low	15(45.5%)	0	<0.001
Moderate	14(42.4%)	5(16.1%)	
High	4(12.1%)	26(83.9%)	
Diabetes*			
Yes	27 (80.6%)	27 (87.1%)	0.82
No	6 (19.4%)	4 (12.9%)	
Hypertension*			
Yes	23 (69.7%)	25 (80.6%)	0.47
No	10 (30.3%)	6 (19.4%)	

≠ Values represented as Mean±Standard deviation.
* Values represented as percentages.

The parameters assessed with regard to obesity were Body Mass Index (BMI) and Waist Hip ratio (WHR). Both BMI and the waist hip ratio were found to be significantly greater in individuals having NAFLD compared to controls. But the p value was more for BMI (p=0.001 OR=6.8 CI =2.07–22.2) as compared to WHR. (p=0.04 OR=2.77 CI=1.0007–7.6)

TABLE II: BMI.

BMI	*Cases (n=33)*	*Controls (n=31)*	*p*	*OR (95% CI)*
High	28 (84.8%)	14 (45.2%)	0.001	6.8 (2.07-22.2)
Normal	5 (15.2%)	17 (54.8%)		

TABLE III: WHR.

WHR	*Cases (n=33)*	*Controls (n=31)*	*p*	*OR (95% CI)*
Normal	12 (36.4%)	19 (61.3%)	0.04	2.77(1.007-7.6)
High	21 (63.6%)	12 (38.7%)		

The biochemical parameters that were compared between the two groups were Fasting Blood Sugar (FBs), Serum Glutamic Oxaloacetic Transaminase (SGOT), Serum Glutamic Pyruvic Transaminase (SGPT), Alkaline phosphatise (ALP), Total Cholesterol, High Density Lipoproteins (HDL), Low Density Lipoproteins (HDL), Triglycerides and Total protein. Out of these only SGPT levels showed significant difference between the two groups with

TABLE IV: Biochemical parameters.

	Cases	*Controls*	*p*	*OR (95% CI)*
FBS				
High	8(24.2%)	5(16.1%)	0.592	1.935(.167-22.5)
Normal	25(75.8%)	26(83.9%)		
SGOT				
High	16(48.5%)	8(25.8%)	0.061	2.706(.942-7.772)
Normal	17(51.5%)	23(74.2%)		
SGPT				
High	22(66.7%)	8(25.8%)	0.001	5.750(1.948-16.968)
Normal	11(33.3%)	23(74.2%)		
ALP				
High	2(6.1%)	1(3.2%)	0.524	1.935(.167-22.482)
Normal	31(93.9%)	30(96.8%)		
Total cholesterol				
High	15(45.5%)	13(41.9%)	0.08	1.154(.429-3.103)
Normal	18(54.5%)	18(58.1%)		
HDL				
High	27(54%)	23(46%)	0.46	1.565(.473-1.574)
Normal	6(42.9)	8(57.1)		
LDL				
High	11(55%)	9(45%)	0.71	1.22(.423-3.53)
Normal	22 (50%)	22(50%)		
Triglycerides				
High	15(45.5%)	8(25.8%)	0.257	2.396(.83-6.89)
Normal	18(54.5%)	23(74.2%)		
Total Protein				
Low	0	1(3.2%)	0.298	–
Normal	33(100%)	30(96.8%)		

NAFLD groups having a high level of SGPT (70.94±73.2) as compared to controls (37.71±32.5) with a *p* value of 0.001(OR=5.75 CI=1.948–16.968).

The physical activity scores as expressed both by MET minutes and categorically as low, moderate and high were significantly high in the control group. The MET score in the NAFLD group was 948.80±628.4 (Mean±SD) compared to the control group of 4475.77±3202.3 (Mean±SD) with a *p* value of <0.001. 26 out of 31 participants in the control group (83.9%) were having high level of physical activity while only 4 out of 33(12.1%) had high level of physical activity in the NAFLD group. Low level of physical activity was reported by 15 out of 33 patients in the NAFLD group as compared to none in the control group. Moderate physical activity levels were reported by 14 out of 33 participants (42.4%) in the NAFLD group and 5 out of 31 participants 5(16.1%) in the control group. The *p* value for the categorical representation also was statistically significant (*p*<0.001).

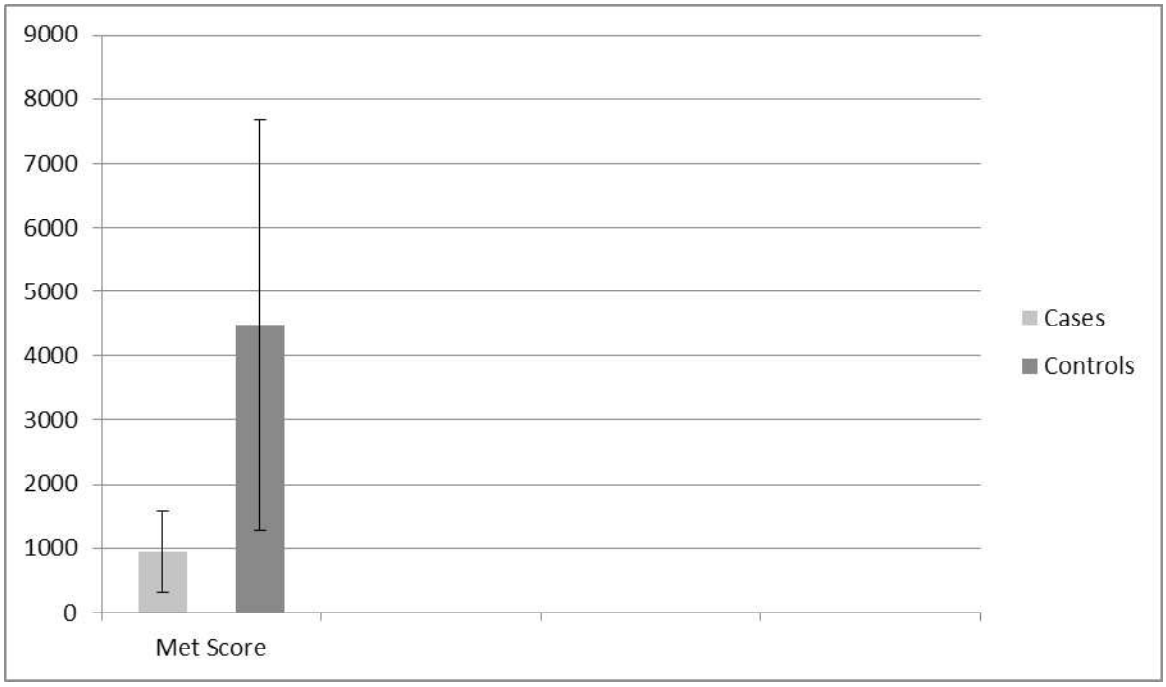
Dietary assessment done with 24-hour dietary recall method showed a significantly excess calories consumed by the NAFLD group with respect to their recommended intake. The calorie consumption in the NAFLD group was 2576.48±364.41 (Mean ± SD) and 2305.19±323.35 (Mean ± SD) in the control group with a p value of 0.003. The macronutrient composition failed to show any difference between the groups. The distributions of diabetic and hypertensive patients between the two groups were also comparable to each other in contrast to the published literature. 27 out of 33 participants (80.6%) had diabetes in the NAFLD group while 27 out of 31 participants (87.1%) reported diabetes in the control

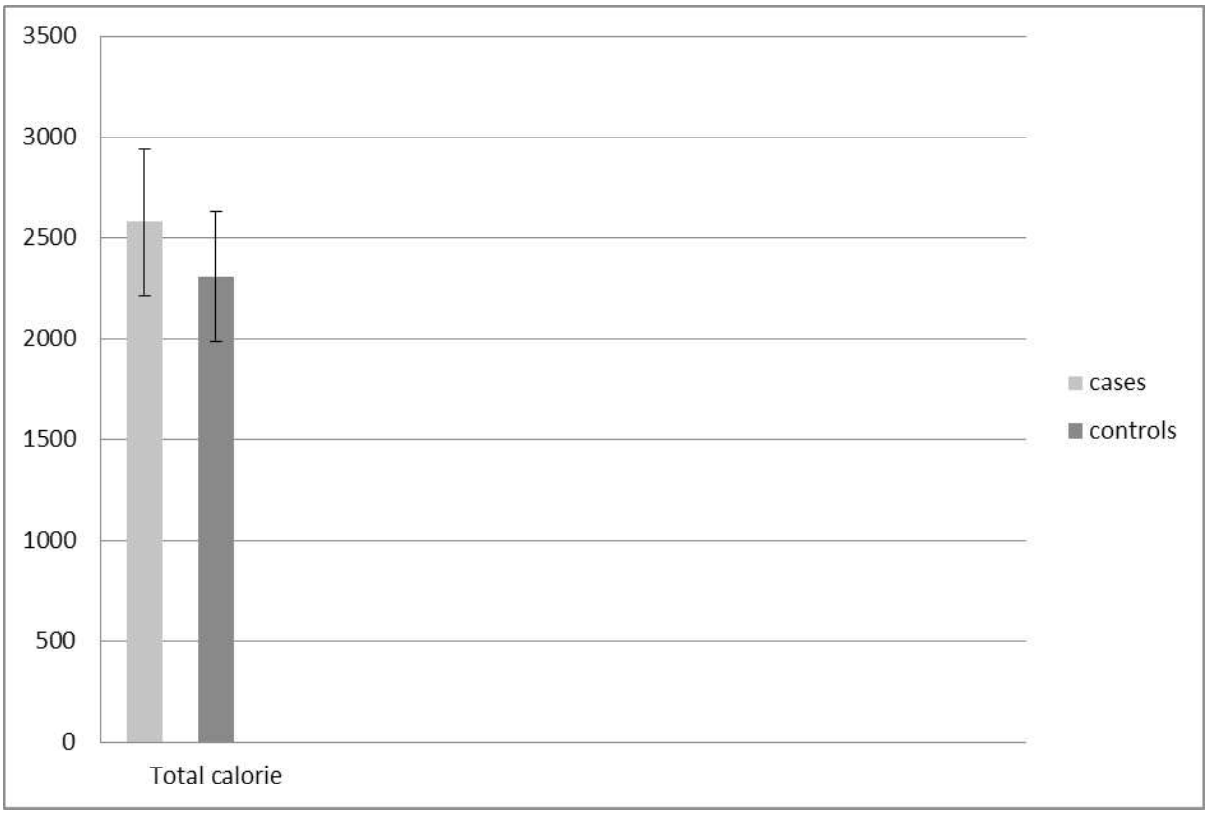
TABLE V: Physical activity scores. (Met scores)

Met score	*Cases (n=33)*	*Controls (n=31)*
Mean±SD	948.80±628.4	4475.77±3202.3
Low	15(45.5%)	0
Moderate	14(42.4%)	5(16.1%)
High	4(12.1%)	26(83.9%)
Inference	Physical activity is significantly high in controls with *p*=<0.001	

TABLE VI: Dietary assessment.

Total calorie intake	*Cases (n=33)*	*Controls (n=31)*
Mean±SD	2576.48±364.41	2305.19±323.35
Inference	Total calorie intake is significantly high in cases with *p*=<0.003	





group. Similarly, 23 out of 33 participants 23 (69.7%) had hypertension in the NAFLD group and 25 out of 31 participants 25 (80.6%) were hypertensive in the control group.

TABLE VII: Distribution of diabetes and hypertension.

	Cases n=33	*Controls n=31*	*p*
Diabetes*			
Yes	27 (80.6%)	27 (87.1%)	0.82
No	6 (19.4%)	4 (12.9%)	
Hypertension*			
Yes	23 (69.7%)	25 (80.6%)	
No	10 (30.3%)	6 (19.4%)	0.47
Inference	There is no significant difference in the distribution of diabetic and hypertensive patients between the two groups		

Discussion

NAFLD is considered as the hepatic equivalent of metabolic syndrome that comes under the group of life style diseases. End stage NAFLD accounts for 4% to 10% of liver transplants in western population, which is on a rapid rise due to the fast-expanding global epidemic of obesity (1).

In the present study level of physical activity showed a strong inverse relationship with NAFLD. The results match well with that of the study conducted by Hiesh et al (18) who concluded that decreased levels of daily physical activity (≤1 day/wk vs ≥3 days/wk) were associated with increased incidence of NAFLD. Similarly, R. Scott Rector and John P. Thyfault (19) have also observed an increased incidence and severity of NAFLD among individuals who do not engage in the upper end of moderate or vigorous physical activities. Zelber-Sagi et al (20). compared the association of aerobic and resistance exercises with the incidence of NAFLD and concluded that the association is stronger with resistance exercises, which remained statistically significant even after correction with body mass index. The same was demonstrated for resistance exercise by Hallsworth et al (21) who demonstrated that regular practice of resistance exercise (3 times a week, for 8 weeks) was effective in reducing intrahepatic lipids in subjects with NAFLD. Supporting data was given by Whitsett

et al (22), in a comprehensive review of eighteen studies; which showed that exercise improved hepatic steatosis and underlying metabolic abnormalities in NAFLD.

Shelby Sullivan (23) in her review examined the effects of excess calories on NAFLD, suggesting that ongoing excess caloric delivery directly contributes to the development of NAFLD. This is well in accordance with the results obtained by our study where a significantly higher calorie intake was observed in the NAFLD group ($p<0.003$). The dietary composition of macronutrients has less established role in the pathogenesis of NAFLD. Although some studies (24) have reported increased incidence of NASH in people whose diet is composed of more calories contributed by fat our study failed to show any significant difference in the macronutrient composition of the diet between two groups.

Obesity was measured by assessing the waist hip ratio and body mass index. Truncal obesity, measured by waist hip ratio, is now being considered as a more important risk factor for NAFLD. The number of subjects having high WHR was significantly more in the NAFLD group in the present study. Similar association between WHR and NAFLD was documented in a case control study conducted by Rui-Dan Zheg et al (25). Comparable results were obtained by Quing Pang et al (26) in a review of twenty studies estimating the influence of central obesity on NAFLD occurrence.

BMI is regarded as an independent predictor of NAFLD. In the present study, (84.8%) of the cases were having a body mass index > 30 kg/m^2 while more than half (54.5%) of the controls had their BMI< 30 kg/m^2. The difference remained statistically significant with a p value <0.001 which is comparable to the data obtained from other studies (12, 14).

As reported by many studies the only biochemical abnormality that was found in our study was elevation of SGPT, with the NAFLD group having abnormally high values of SGPT as compared to controls (15, 16).

One of the limitations of the study is that, we have not considered the radio-diagnostic changes as ultrasound imaging was used only for the diagnosis, i.e. presence or absence of NAFLD.

Conclusion

The following conclusions could be derived from the present study.

- Physical activity has a strong inverse relationship with NAFLD.
- NAFLD increases with low physical activity level
- Excess calorie intake has a strong positive correlation with NAFLD.
- Obese individuals are relatively at a higher risk of having NAFLD than the non-obese.
- NAFLD is associated with increased levels of Serum Glutamic Pyruvic Transaminase (SGPT), while no such correlation was observed with Serum Glutamic Oxaloacetic Transaminase (SGOT).
- Serum lipid profile has no significant association with NAFLD.

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