

Comparison of Physical Activity and Fiber and Sugar Intake in Patients with Nonalcoholic Fatty Liver Disease with Healthy Individuals

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ABSTRACT

Introduction: Nutrition is a modifiable risk factor, which plays a key role in the prevention or delayed onset of non-alcoholic fatty liver disease (NAFLD). The present study aimed to assess and compare the physical activity and dietary intake of fiber and sugar between patients with NAFLD and healthy individuals.

Methods: This case-control study was conducted on 225 patients with NFDL and 450 healthy controls. The physical activity and dietary intakes of the subjects were assessed using the International Physical Activity Questionnaire and Food Frequency questionnaire, respectively. In addition, the anthropometric indices of the subjects were determined, including weight, height, body mass index (BMI), and waist-to-hip ratio. Data analysis was performed in SPSS version 21.0.

Results: The level of physical activity in the patients with NAFLD was lower compared to the controls ($P < 0.05$). Regarding insoluble dietary fiber, the consumption was significantly lower in the case group compared to the control group ($P < 0.05$). Moreover, the levels of fructose, galactose, total sugar, and glucose significantly increased in the case group ($P < 0.05$).

Conclusion: According to the results, adherence to unhealthy diets with the high consumption of simple carbohydrates (e.g., glucose, fructose, and galactose) may be associated with the incidence of NAFLD. On the other hand, consumption of dietary fiber and insoluble fiber may exert protective effects against NAFLD.

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Introduction

Non-alcoholic fatty liver disease (NAFLD) is a disorder in which triglyceride is accumulated in the liver cells of the individuals with no history of alcohol consumption or those seldom consuming alcohol.(1) NAFLD has a wide spectrum, and many of the patients may only have increased fat in the liver tissues, which is referred to as simple steatosis. However, some of these cases may progress toward non-alcoholic steatohepatitis, exposing the patient to the risk of hepatic fibrosis, cirrhosis, and even hepatocellular carcinoma.(2)

The prevalence of NAFLD in the Mediterranean region has been reported to be 36.8%, while is

estimated at 20-40% in Europe, 9-30% in Japan, and 16-32%, and 9% in the urban and rural areas of India, respectively. It is notable that the lowest prevalence rate of the disease has been reported in Asian countries (5% in Singapore). (3, 4) In Iran, the prevalence of NAFLD has been estimated at 2.9-7.1% in the general population.(5)

With regard to etiology, NAFLD is a multi-dimensional disease, and several factors are known to intervene in its incidence, such as genetics and lifestyle (e.g., nutrition and physical activity).(6) Currently, no approved pharmacological therapies are available for

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NAFLD, and the treatment is primarily focused on lifestyle modifications, including weight loss, dietary changes, and increased physical activity.(7)

Diet and micronutrients are among the main influential factors in the incidence of NAFLD, which have attracted the attention of researchers. For instance, adherence to diets with high dietary carbohydrate contents via the *de novo* synthesis of fatty acids and increasing of blood triglycerides have been shown to be effective in the incidence of NAFLD.(8) Furthermore, the consumption of non-alcoholic drinks with high sugar content are associated with obesity in children and adolescents, (9) and recent evidence suggests that the correlation between such beverages and risk of obesity and diabetes is due to the excessive amount of fructose corn syrup, which increases triglyceride and blood sugar levels.(9) On the other hand, recent data have indicated that high consumption of fructose could increase the fat mass, lipogenesis, and inflammation.(10)

Soluble and insoluble dietary fibers are both beneficial in the prevention of diabetes through reducing the glucose response after meals, as well as the improvement of some part of the lipid profiles. To date, few studies have been focused on the effects of fibers on NAFLD in animals and humans, while studies regarding diets have proposed proper findings on the correlation between fiber intake and NAFLD.(11, 12)

Physical activity plays a pivotal role in the promotion of health status and body composition, as well as the reduction of the risk of obesity.(13) Inadequate physical activity is a significant risk factor for cardiovascular diseases, NAFLD, and type II diabetes mellitus. Physical activity is influenced by the socioeconomic status and demographic changes over time.(14) In a study in this regard, Kistler et al. reported an inverse correlation between vigorous-intensity physical activity and NAFLD severity.(15) Moreover, it has been claimed that high-energy diets are often associated with high rates of fat and low rates of fibers. Dietary fats increase energy per each weight unit, requiring lower energy to be metabolized.(16)

The previous studies in this regard have been limited, proposing scarce evidence. Considering that nutrition plays a key role in the incidence of NAFLD, as well as the lack of mobility and overall decline in the physical activity of the

general population, the present study aimed to assess a wide range of dietary components and their effects on NAFLD, while the increased prevalence of noninvasive diseases (especially NAFLD) has further necessitated the investigation of this issue.

Materials and Methods

This case-control study was conducted on 225 patients with NAFLD (case) and 450 healthy controls at the Metabolic Diseases Research Center, affiliated to Isfahan University of Medical Sciences, Iran during December 2018-May 2019. The study protocol was approved by the Ethics Committee of Isfahan University of Medical Sciences, and written informed consent was obtained from the participants prior to enrollment.

The case group included the individuals with the confirmed diagnosis of NAFLD via sonography by a specialist, and the control group consisted of the individuals with normal sonography results after referral to the center for various reasons. The inclusion criteria of the study were the presence of NAFLD based on laboratory tests, sonography results, and diagnosis by a radiologist, age of 20-60 years, and consent for participation. The excluding criteria were as follows: 1) history of previous/recent alcohol consumption; 2) adherence to low-calorie diets within the past two months; 3) patients with alcoholic hepatitis, autoimmune hepatitis, and viral hepatitis; 4) history of primary biliary cirrhosis and biliary obstruction; 5) patients with metabolic liver diseases (e.g., Wilson's disease and hemochromatosis) and 6) history of using effective liver medications.

After the calculation of the consumed energy of the participants, those receiving less than 800 kilocalories or more than 4,200 kilocalories of energy per day were excluded from the study.

Data were collected using a questionnaire consisting of two sections; the first section contained data on demographic characteristics (age, gender, marital status, and family history of NAFLD) and the health behaviors related to lifestyle (e.g., alcohol consumption, smoking habits), and the second section contained data on the measurement of height, weight, waist circumference, and hip circumference.

In order to assess the rate of physical activity, we used the Short-form International Physical Activity Questionnaire (IPAQ).(17) The rate was divided into three categories, including limited

physical activity (if the subject did not meet the inclusion criteria for intermediate/intense levels of physical activity), intermediate physical activity (if the subject had intense physical activities for a minimum of 20 minutes per day for three days or more or if had at least 30 minutes of intermediate physical activities/walking five days per week or more), and intense physical activity (if the subject had intense physical activity for a minimum of three days [equivalent to the minimum of 1,500 MET/min/week] or if the subject had combined walking/intermediate/intense physical activity seven days per week, reaching the minimum of 3,000 MET/min/week).

Evaluation of Food Intake

Data on the usual nutrition of the subjects were confirmed using the semi-quantitative food frequency questionnaire (FFQ) with 168 items.(18) FFQ has a list of common Iranian meals with the standard serving sizes, and the consumption frequency of the foods is divided into nine categories. The participants determined their consumed diet within the past year by selecting various options, including Never/Less than Once a Month, 3-4 Times a Month, Once a Week, 5-6 Times a Week, Once a Day, 2-3 Times a Day, 4-5 Times a Day, and ≥6 Times a Day.

At the next stage, the foodstuffs were evaluated in terms of their ingredients, the amounts of which were calculated in grams. Afterwards, the energy rates of the micronutrients and macronutrients were calculated using the

Nutritionist 4 software (First Databank Inc., Hearst Corp., San Bruno, CA).

Statistical Analysis

Data analysis was performed in SPSS version 21 (SPSS Inc., Chicago, IL, USA). The quantitative data were expressed as mean and standard deviation, and the qualitative data were expressed as numbers and percentages. The Kolmogrov-Smirnov test was used to determine the normality of the data, and the associations between the disease and qualitative data were evaluated using Chi-square. In addition, the quantitative data were compared between the groups using independent t-test and analysis of covariance.

Results

Comparison of Demographic Characteristics between the Case and Control Groups

Table 1 shows the frequency distribution of the demographic characteristics in the case and control groups. According to the results of the Kolmogrov-Smirnov test, all the quantitative variables had normal distribution, and the independent t-test was used to compare the demographic characteristics between the case and control groups. No significant differences were observed between the groups in terms of age and gender (P>0.05). On the other hand, the variables of height, weight, waist-to-hip ration (WHR), and body mass index (BMI) were significantly higher in the case group compared to the control group (P<0.05). In addition, comparison of physical activity indicated that the case group had lower activity compared to the controls (P<0.05).

Table 1. Comparison of demographic Characteristics and Physical Activity between Case and Control Groups

Variable	Case N=225	Control N=450	P-value
#Gender			
	N (%)		0.35
Male	125 (55.6)	233 (51.8)	
Female	100 (44.4)	217 (48.2)	
#Physical Activity			
Low (<600)	178 (79.1)	267 (59.3)	0.001***
Moderate (600-1,500)	43 (19.1)	133 (29.6)	
High (>1,500)	4 (1.8)	50 (11.1)	
#Smoking Habits			
No	209 (92.9)	438 (97.3)	0.12
Yes	16 (7.1)	12 (2.7)	
#Alcohol Consumption			
No	194 (86.2)	404 (89.8)	0.07
Yes	31 (13.8)	46 (10.2)	
Age (year)**	38.6±8.7	37.8±8.9	0.29
Height (cm)**	165.4±10.4	162.1±9.3	0.001***
Weight (kg)**	83.3±10.6	65.5±8.8	0.001***

BMI* (kg/m ²)**	30.5±4.02	24.9±3.09	0.001***
WHR**	0.97±0.06	0.87±0.06	0.001***
MET	1119.03±616.3	1590.30±949.4	0.001***

Variables expressed as mean±SD; **In normal variables, independent samples t-test used; #Chi-square used for comparison of groups; *BMI=body mass index; ***Significant difference between groups (P<0.05)

Comparison of Fiber Intake between the Case and Control Groups

According to the information in Table 2, the study groups had no significant differences in

terms of the intake of soluble fibers and crude fibers (P>0.05). However, the intake of insoluble dietary fibers was significantly lower in the case group compared to the controls (P<0.05).

Table 2. Consumption of Dietary Fiber in Case and Control Groups

Variable	Case N=225	Control N=450	P-value
Energy (kcal/day)	2315.4±606.5	2170.5±622.5	0.005*
Total Dietary Fiber (g/day)	35.4±18.1	39.8±23.07	0.025*
Soluble Fiber (g/day)	0.51±0.33	0.54±0.42	0.19
Insoluble Fiber (g/day)	2.4±1.4	3.5±1.8	0.006*
Crude Fiber (g/day)	9.9±5.7	10.6±10.4	0.65

Variables expressed as mean±SD; *Significant difference between groups (P<0.05); Case and control groups adjusted for age, gender, physical activity, BMI, and energy using analysis of covariance (ANCOVA)

Comparison of Dietary Carbohydrate Intake between the Case and Control Groups

Table 3 shows the mean values of dietary carbohydrate intake in the case and control groups. Accordingly, the study groups had no significant differences in the variables of

maltose, lactose, and sucrose (P>0.05). However, the levels of fructose, galactose, total sugar, and glucose significantly increased in the case group compared to the control group (P<0.05).

Table 3. Comparison of Dietary Carbohydrates between Case and Control Groups

Variable	Case N=225	Control N=450	P-value
Glucose (g)	17.9±9.1	15.2±8.6	0.032*
Galactose (g)	3.7±2.7	3.2±2.3	0.023*
Fructose (g)	18.9±11.5	17.5±9.8	0.048*
Sucrose (g)	30.2±15.8	31.9±22.3	0.055
Lactose (g)	16.05±10.4	16.2±10.9	0.063
Maltose (g)	1.4±1.2	1.3±0.86	0.94
Sugar (g)	118.6±46.1	115.8±48.7	0.002*

Variables expressed as mean±SD; *Significant difference between groups (P<0.05); Case and control groups adjusted for age, gender, physical activity, BMI, and energy using ANCOVA

Discussion

According to the results of the present study, physical activity was significantly lower in the patients with NAFLD compared to the control group. Previous studies have indicated that the primary action for the treatment of NAFLD is lifestyle modification, which encompasses gradual weight loss and increased physical activity.(19) Lifestyle changes (e.g., increased independent physical exercises) positively influence NAFLD patients.(20)

The findings of the current research demonstrated that the intake of total dietary fibers and insoluble fibers was higher in the healthy controls compared to the patients with NAFLD. Few studies have been focused on the effects of fiber on animals and humans with NAFLD. However, a similar research performed in the United States on animal samples indicated

that the rate of intrahepatic triglyceride reduced with the increased consumption of nutritional fiber.(21)

A study conducted on children demonstrated that the consumption of foods with high rates of carbohydrates and saturated fatty acids and low fiber intake are positively correlated with NAFLD pathogenesis.(22) Therefore, it could be inferred that low fiber intake is correlated with higher BMI, fat accumulation, and higher rates of lipid serum.(23) Moreover, consumption of dietary fiber and its effects on NAFLD could be attributed to the reduction of low-density lipoprotein, insulin resistance, and fat accumulation in the body.(24)

According to the results of the present study, the intake of total sugar was lower in the healthy controls compared to the NAFLD patients, while this rate was higher in the NAFLD patients in terms of other carbohydrates, such as glucose,

fructose, and galactose, denoting a significant difference in this regard. It is notable that few studies have been focused on the correlation between dietary carbohydrates and NAFLD.

According to the findings of Metin Basaranoglu et al., the increased consumption of beverages with high sugar contents (sweetened beverages) is associated with the risk of metabolic syndrome, and corn syrup with its high fructose content could also increase *de novo* synthesis, thereby increasing the risk of NAFLD.(25)

In another research, Guenther Silbernagel et al. claimed that diets with high glucose and fructose contents may reduce insulin sensitivity, while the consumption of fructose could also increase serum triglyceride levels.(26) Another study in this regard has also demonstrated that the increased intake of simple carbohydrates is associated with the extensive development of NAFLD.(11, 27)

Some studies have shown that BMI has a negative, inverse, significant correlation with the grades of physical components and physical performance in patients with chronic liver diseases, while these patients also have increased immobility.(28)

According to the findings of the current research, the weight and BMI were higher in the case group compared to the control group. According to the research by Radu et al., BMI was significantly higher in the patients with fatty liver compared to the controls.(29) Therefore, the high rate of BMI could be considered an independent predictive factor for NAFLD.(30)

In the current research, the WHR was higher in the case group compared to the control group, and the correlation was considered significant. Consistently, Rui-Dan Zheng reported that the WHR was significantly correlated with the incidence of NAFLD, while it could also predict the disease. Another study regarding the WHR indicated that abdominal obesity may be a severe health threat as opposed to general obesity although disorders may independently increase the risk of NAFLD.(31)

The limitations of the present study were as follows:

1. Diagnosis of NAFLD was based on sonography results although the 'gold standard' diagnostic method was applied in case of percutaneous liver biopsy.

2. Due to the possible biases in case-control and retrospective studies, it is recommended that the disease risk factors be further evaluated in futuristic studies on various populations.

3. The self-report of the participants might have been faulty in some cases in the FFQ and physical activity questionnaires.

The strengths of the study were as follows:

1. Large sample size compared to previous studies;
2. Using the 168-item FFQ for the analysis of diets;
3. Case-control design for the assessment and comparison of the disease risk factors as opposed to cross-sectional studies

Conclusion

According to the results, adherence to unhealthy diets involving the high consumption of simple carbohydrates (e.g., glucose, fructose, and galactose) might be associated with the incidence of NAFLD. However, consumption of dietary fiber and insoluble fibers could exert protective effects against NAFLD.

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