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Adherence to the Mediterranean diet is associated with the severity of non-alcoholic fatty liver disease☆

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SUMMARY

Background & aims: Nutrition has been proposed as a potential environmental factor affecting the risk of non-alcoholic fatty liver disease (NAFLD). In the present study, the impact of adherence to the Mediterranean diet (MD) on the presence and severity of NAFLD was explored.
Methods: Seventy-three consecutive adult patients with recent NAFLD diagnosis were included. Adherence to the MD was estimated with MedDietScore. Demographic and anthropometric data, body composition analysis and several biochemical and inflammatory markers were estimated. Liver stiffness measurements by transient elastography were available in 58 patients and liver biopsies in 34 patients. Fifty-eight patients were matched with 58 healthy controls in terms of age, sex and body mass index.
Results: MedDietScore was negatively correlated to patients' serum alanine aminotransferase ($p = 0.03$) and insulin levels ($p = 0.001$), insulin resistance index ($p = 0.005$) and severity of steatosis ($p = 0.006$) and positively to serum adiponectin levels ($p = 0.04$). Patients with non-alcoholic steatohepatitis (NASH) exhibited lower adherence to MD (29.3 ± 3.2 vs. 34.1 ± 4.4, $p = 0.004$) compared to those with simple fatty liver. Logistic regression analysis revealed that one unit increase in the MedDietScore was associated with 36% lower likelihood of having NASH (odds ratio: 0.64, 95% confidence interval: 0.45–0.92), after adjusting for sex and abdominal fat level. No difference in the MedDietScore was observed between patients and controls.
Conclusions: Higher adherence to the Mediterranean diet is not associated with lower likelihood of having NAFLD, but it is associated with less degree of insulin resistance and less severe liver disease among patients with NAFLD.

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) represents the most common chronic liver disease in Western countries.[1] NAFLD is the result of fat accumulation in the liver (liver fat >5–10% of liver weight) which is not due to excess alcohol consumption or other causes of steatosis, while its severity ranges from simple hepatic steatosis or fatty liver to non-alcoholic steatohepatitis (NASH).[1] NAFLD is considered as the hepatic manifestation of the metabolic syndrome with insulin resistance being the most prevailing pathogenetic mechanism.[2] Dysregulations of proinflammatory cytokines and adipokines are almost universally detected in NAFLD patients, while oxidative stress and apoptosis appear to contribute to the development of NASH.

Both genetic and environmental factors have been proposed to be implicated in the etiology of NAFLD. Thus, nutrition is reasonably

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BIA, bioelectrical impedance analysis; FFQ, food frequency questionnaire; GGT, gamma-glutamyl transpeptidase; HDL, high density lipoprotein; hsCRP, high sensitivity C-reactive protein; IL-6, interleukin-6; IL-8, interleukin-8; LDL, low density lipoprotein; LSM, liver stiffness measurements; MedDietScore, Mediterranean Diet Score; NAFLD, non-alcoholic fatty liver disease; NAS, NAFLD activity score; NASH, non-alcoholic steatohepatitis; TGF-β1, transforming growth factor beta-1; TNF-α, tumor necrosis factor-α; VEGF, vascular endothelial factor.

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considered to be a potential environmental factor affecting the risk for this disease.[3] The impact of both positive energy balance and diet's composition on the risk and the stage of NAFLD have been explored, mainly through retrospective observational studies. Although there is consistent evidence that overweight due to energy overconsumption increases the risk for and the prevalence of NAFLD,[4] the role of diet's composition, in terms of macro- or micronutrients, in the pathogenesis of the disease remains controversial.[5]

Current trends in clinical nutrition and nutritional epidemiology propose that pattern analysis, examining the effects of the overall diet, is the most realistic approach to examine associations between diet and disease instead of looking at individual nutrients or foods and food groups.[6] Mediterranean diet is a dietary pattern that has been extensively associated with favorable health outcomes, mainly in relation to mortality, cardiovascular disease risk factors and cancer.[7] In relation to the metabolic syndrome, according to a recent systematic review and meta-analysis,[8] adhering or adopting a Mediterranean dietary pattern has a beneficial effect both on the prevention and the resolution of the metabolic syndrome, as well as on individual metabolic parameters. To our knowledge, there are no epidemiological or clinical data on the impact of the Mediterranean diet on the risk for and stage of NAFLD.

The aim of this study was to explore any potential associations between adherence to the Mediterranean diet and the clinical and histological characteristics of patients with NAFLD. A control group was also enrolled to explore any potential involvement of the adherence to the Mediterranean diet in the presence of NAFLD.

2. Materials and methods

The study sample consisted of 73 consecutive adult (18–65 years old) patients with recent (within the last 6 months) diagnosis of NAFLD, who visited the outpatient liver clinics of the 2nd Academic Department of Internal Medicine at Hippokration General Hospital of Athens between May 2009 and December 2010. Participants included were free of diabetes mellitus and liver neoplasm. NAFLD was diagnosed in patients who met all the following criteria: abnormal alanine aminotransferase (ALT) and/or gamma-glutamyl transpeptidase (GGT), ultrasonographic evidence of hepatic steatosis and/or compatible liver histology, and no other cause of liver injury and steatosis. In particular, all patients should have had negative serological markers for hepatitis B (HBsAg), hepatitis C (anti-HCV) and human immunodeficiency virus (anti-HIV), weekly alcohol consumption less than 210 g for men or 140 g for women, no use of potentially hepatotoxic agents, no evidence of metabolic or autoimmune liver disease, and absence of any known systemic disease with potential liver involvement. In addition, patients who had changed their habitual eating habits since NAFLD diagnosis and those following a weight loss diet, as well as patients with diabetes mellitus and/or any diagnosed malignancy were excluded from the study. Medical records were thoroughly reviewed and laboratory data were recorded, namely complete blood count, prothrombin time, uric acid, urea, creatinine, liver enzymes [ALT, aspartate aminotransferase (AST), alkaline phosphatase, GGT, total protein, albumin], serum copper, ceruloplasmin, iron and ferritin, as well as detection of HBsAg, anti-HBc, anti-HBs, anti-HCV, anti-HIV, liver autoantibodies (anti-nuclear, anti-smooth muscles, anti-microsomial, anti-mitochondrial). Participants' habits such as smoking, alcohol consumption and reception of any medication were also recorded. The history of alcohol use was taken from the patients and was confirmed by the patients' relatives or friends.

Moreover, 58 healthy controls matched for age, sex and BMI with 58 patients were evaluated. Controls were either subjects who visited the outpatient clinics of the same department during the study period for routine examinations or people working at the same Department and the universities involved in the study. Controls had stable dietary and exercise habits during the last year and normal liver enzymes. Moreover to minimize the selection bias they underwent ultrasonography to confirm the absence of hepatic steatosis. For all the controls, dietary, physical activity, body composition and biochemical assessments were conducted. The study was approved by the Ethics Committee of the Hippokration General Hospital of Athens and by the Ethics Committee of Harokopio University and was carried out in accordance with the Declaration of Helsinki.[9] All participants were informed about the aims and procedures of the study and gave their written consent.

2.1. Dietary & physical activity assessment

Participants' habitual dietary intake over the last 12 months was assessed through a 60 items semi-quantitative food frequency questionnaire (FFQ), enriched with foods and beverages commonly consumed in Greece.[10] Based on the FFQ data, dietary intake was expressed in terms of food groups (e.g. dairy foods, fruits, vegetables) and individual foods and beverages (e.g. nuts, potatoes, beverages). To evaluate the level of adherence to the Mediterranean dietary pattern the Mediterranean Diet Score (MedDietScore) was used.[11] In particular, for the score calculation, the consumption of food items from 9 food groups (non-refined starchy food, potatoes, fruit, vegetables, legumes, fish, meat and meat products, poultry, and full fat dairy products), as well as olive oil, and alcoholic beverages, were taken into account. For the consumption of food items that are close to this dietary pattern, a score 0 was assigned for no consumption, and scores 1 to 5 for rare to daily consumption, respectively. On the other hand, for the consumption of foods that are away from this pattern, the opposite scores were assigned (i.e. 0 for almost daily consumption to 5 for rare or no consumption). Consumption of various alcoholic beverages was calculated in wine glasses of 100 mL and 12-g ethanol concentrations. For alcohol, score 5 was assigned for consumption of less than 300 ml/day, score 0 for consumption of more than 700 ml/day or 0 ml/day and scores 1 to 4 for consumption of 600–700, 500–600, 400–500 and 300–400 ml per day, respectively. The range of the MedDietScore is 0–55. Higher values of the dietary score indicate greater adherence to the Mediterranean diet.

Physical activity level of the participants was assessed trough a questionnaire that has been previously used in adults.[12,13] Briefly, the questionnaire recalls previous day's physical activities by recording the duration, the type and the intensity of each activity, as well as time spent daily in television viewing or computer use. Based on this information, daily time spent in moderate and vigorous activities (structured or not) and in sedentary activities were calculated. Participants were also given a pedometer (Digi-Walker, Yamax, SW-200, Japan) for a 7-day period (including weekend days) and each participant was asked to record his/her daily steps according to the measurements appearing on the pedometer screen.

2.2. Anthropometric & body composition assessment

Body weight of participants was measured with digital scale (Seca robusta 813, Hamburg, Germany), to the nearest 100 g and height to the nearest 0.5 cm. The body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Waist circumference was tape measured to the nearest 0.1 cm.

Abdominal fat compartments, namely trunk fat % and abdominal fat level were estimated by abdominal bioelectrical impedance analysis (Tanita Viscan AB140, Japan).[14]

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