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Dietary patterns and non-alcoholic fatty liver disease in a Greek case–control study

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ABSTRACT

Objective: The aim of this study was to test the hypothesis that posteriori-derived dietary patterns of a Greek sample are associated with the odds for non-alcoholic fatty liver disease (NAFLD) and common NAFLD-related biomarkers.

Methods: We recruited 351 individuals (134 NAFLD patients, 217 controls). NAFLD was diagnosed with abdominal ultrasound. Dietary intake data were collected through a semi-quantitative food frequency questionnaire of 172 items and dietary patterns were derived by factor analysis. Consumption of dietary patterns was divided into quartiles. Multivariate logistic and linear regression models were applied to investigate associations of dietary patterns with NAFLD odds and common NAFLD-associated biomarkers.

Results: Four dietary patterns were identified. Adherence to the fast food–type dietary pattern was independently associated with higher odds for NAFLD. However, results were statistically significant only for the highest versus the lowest consumption (odds ratio, 3.9; $P = 0.003$). On the contrary, individuals in the second quartile of the unsaturated fatty acid dietary pattern had 55.7% reduced odds of developing NAFLD than those in the first quartile after adjusting for age, sex, energy intake, physical activity level, pack-years smoked, education years, and presence of metabolic syndrome ($P = 0.039$). The fast food–type pattern was further associated with higher levels of C-reactive protein and uric acid and the unsaturated fatty acid pattern with reduced levels of insulin and homeostatic model assessment of insulin resistance ($P < 0.05$). The prudent dietary pattern was associated with decreased triacylglycerol and uric acid levels ($\beta = -5.960$; $P = 0.037$ and $\beta = -0.153$; $P = 0.035$, respectively).

Conclusion: This is the first study to indicate associations of dietary patterns with NAFLD in a European population.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is considered a potential new component of metabolic syndrome (MetS) [1]. It is characterized by excessive flux of fatty acids (FA) and triacylglycerol (TG) accumulation in the liver, primarily activated by dietary factors, obesity, and insulin resistance [2]. This results in increased inflammation and mitochondrial dysfunction in the liver—conditions that lead to fibrosis and cell apoptosis. Moreover, genetic and epigenetic factors, and gut microbiome dysfunction, further induce hepatic steatosis, inflammation, and oxidative stress. This multiple-hit model of NAFLD pathogenesis indicates the complexity of the disease and highlights the need to control liver and systemic inflammation.

As mentioned previously, diet is a major contributor to the pathogenesis of NAFLD but it also is an integral part of its treatment [3]. Overall, maintaining a normal body weight and a balanced diet has been shown to reduce inflammation and promote health. Regarding NAFLD, previous studies have demonstrated that excessive energy intake is a key determinant of disease onset and progression [4]. Increased consumption of fat, especially saturated fatty acids (SFA), and simple sugars also have been positively associated with the disease [5]. On the other hand, energy restriction, high protein, high ω-3 polyunsaturated fatty acids (PUFA), and antioxidants intake have been inversely associated with hepatic steatosis.

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Many epidemiologic studies have examined the effect of single nutrients or foods on the risk for NAFLD; however, only a few have investigated the role of diet as a whole. Greater adherence to the Mediterranean diet decreases the risk for NAFLD and NAFLD-related diseases, but it also is believed to reduce the severity of the disease [6,7]. The Mediterranean diet mainly consists of plant foods, fish, and low amounts of red meat. These food groups are rich in antioxidant vitamins and minerals, ω-3 PUFA, and dietary fibers, which are believed to be the components that give the Mediterranean diet its beneficial properties. On the other hand, dietary patterns characterized by increased consumption of red meat, fast foods, sweets, refined cereals, and sweetened soft drinks are rich in processed sugars and fat and have been associated with higher risk for NAFLD [8–10].

To our knowledge, there are no available data regarding dietary patterns of European patients with NAFLD. Against this background, the aim of this study was to assess a posteriori-derived dietary patterns of Greek patients with NAFLD and controls and to estimate the effect of these patterns on disease and its parameters.

Materials and methods

Study population

Study participants were randomly and consecutively recruited from volunteers visiting the Outpatient Clinics of the First Department of Propaedeutic Medicine, Laiko General Hospital, from June 2012 to February 2015. Adults with no self-declared concomitant liver injury at the time of recruitment (viral, autoimmune, genetic, or drug-induced), and no self-declared excessive alcohol intake were screened for the disease. We excluded individuals meeting the following criteria:

- >65 y of age,
- Presence of congenital or acquired liver disease, chronic viral hepatitis, or exposure to hepatotoxic drugs
- Daily consumption of ethanol >20 g for women and >30 g for men
- Coexistence of a life-threatening disease or psychiatric disorder impairing the patient's ability to provide written informed consent
- Pregnant or lactating women.

After applying the exclusion criteria, 351 individuals of Caucasian origin were recruited. This sample size provided 80% power to detect the effect of diet on NAFLD, with an odds ratio of 2. All study participants were informed about the aims of the study and signed a written consent. This study was approved by the Ethics Committee of Harokopio University of Athens, based on the Helsinki Declaration. Detailed methodology of the study has been described previously [11].

NAFLD diagnosis and classification

Participants were screened for NAFLD in the Radiology Department of the hospital. All volunteers underwent an abdominal ultrasound, performed by the same operator throughout the study period. Diagnosis of NAFLD was based on three parameters:

- Diffuse echogenicity of the liver
- Increased echogenicity compared to the renal cortex
- Loss of definition of the diaphragm and blurring of the vascular margins [12].

Screened individuals were initially classified into four groups: absence of hepatic steatosis (normal echogenicity), mild hepatic steatosis (mildly increased echogenicity, normal diaphragm and vascular margins definition), moderate hepatic steatosis (moderately increased echogenicity, mild loss of diaphragm and vascular margins definition), and severe hepatic steatosis (severely increased echogenicity and loss of diaphragm and vascular margins definition). Owing to metabolic and clinical profiles that were not statistically different, individuals with no and mild hepatic steatosis were further classified as controls, whereas individuals with moderate and severe hepatic steatosis were classified as cases. This classification allows depiction of the major contributors to NAFLD development.

Data collection

On the day of recruitment, participants were interviewed regarding their demographic characteristics and family and individual medical history. Their health profile was further assessed by blood tests and blood pressure (BP) measurements. Moreover, anthropometric and body composition measurements, in addition to smoking and physical activity habits, were reported. Repeated measurements of BP and anthropometric variables reduced the risk for bias. Pack-years smoked were calculated for each individual using the formula:

$$\text{number of pack–years} = (\text{number of cigarettes smoked per day}/20) \times \text{number of years smoked}.$$

Physical activity information was collected by the validated short self-reported questionnaire Athens Physical Activity Questionnaire [13]. MetS diagnosis was based on the following criteria: waist circumference (102 cm for men or 88 cm for women); fasting blood glucose >100 mg/dL or previously diagnosed type 2 diabetes; TGs >150 mg/dL or current treatment for this abnormality; BP >130/85 mm Hg or treatment for previously diagnosed hypertension); high-density lipoprotein (HDL) <40 mg/dL for men or <50 mg/dL for women or specific treatment for this abnormality [14]. Patients meeting three of these criteria were considered to have MetS.

Dietary habits

Dietary habits were assessed by a semi-quantitative self-reported food frequency questionnaire (FFQ), which provided information about the consumption of 172 food items during the past year [15]. Portion sizes were reported based on photos and servings. The FFQ was adapted to the dietary habits of the Greek population; therefore it reflected more accurately the actual dietary intake of the present sample. Nutritionist Pro version 2.2 software (Axxya Systems-Nutritionist Pro, Stafford, TX, USA) was used to analyze nutritional information. All self-reported information was double-checked by well-trained dietitians to eliminate under- and overreporting of dietary intake. Dietary information was summarized into food groups.

Factor analysis (principal components [PCA]) was applied to derive dietary patterns for the study population. Analysis was based on the frequency of daily consumption of 15 food groups. The eigenvalues and the scree plot were used to decide on the number of factors retained. Varimax rotation was used and Kaiser–Meyer–Olkin (KMO) index and Bartlett's sphericity test were applied to check the adequacy of the data. Factor loadings < |0.3| were excluded. Dietary patterns were named based on the characteristics of the included food groups. Dietary patterns were further divided into quartiles, where quartile 1 represented low intake and quartile 4 represented high adherence to the dietary pattern. Quartiles of adherence allow for better evaluation of dietary intake.

Statistical analysis

Categorical variables are expressed as frequencies (%), continuous parametric traits as mean values ± standard deviation, and non-parametric variables are described as median [IQR]. To compare mean differences between groups, χ^2 test (categorical variables), independent sample t test (parametric continuous variables), and Mann–Whitney test (non-parametric continuous variables) were performed. Association of each dietary pattern with disease risk was tested with binary logistic regression models, adjusted for the main confounding factors. Linear regression models were applied to identify associations between the dietary patterns' z-scores and NAFLD-associated biochemical parameters. All tests were two-sided and the cutoff level of significance was defined at 0.05. Statistical analyses were performed using SPSS version 21 (IBM, Armonk, NY, USA).

Results

The present sample consisted of 134 patients with NAFLD and 217 controls. The main characteristics of the sample are presented in Table 1. Patients were older, less educated, less physically active, and smoked more than controls ($P < 0.05$). Moreover, the patients had a higher prevalence of obesity and MetS and had higher levels of disease-related biochemical markers than controls ($P < 0.05$).

The following four dietary patterns derived from the factor analysis:

- The fast food–type pattern consisted of energy-dense foods rich in saturated fat and sugar and included fast foods, sweetened soft drinks, fried potatoes, and savory and puff pastry snacks.

Table 1
Characteristics of NAFLD cases and controls

Variables	Cases (n = 134)	Controls (n = 217)	*P*-value*
Sex (% males)	45.5	39.2	0.144
Age (y)	50.4 ± 10.5	43.8 ± 11.2	<0.001
Education years	14 ± 4	15.3 ± 3.6	0.005
PAL	1.4 ± 0.2	1.4 ± 0.2	0.011
Pack-years	15.2 ± 24.5	8.1 ± 13.7	0.024
BMI (kg/m^2)	31.1 ± 4.7	24.9 ± 3.3	<0.001
MetS (yes %)	59	11.5	<0.0001
CRP (mg/L)	2.3 [1.8]	2.2[0.1]	<0.001
FPG (mg/dL)	93.3 ± 12.7	84.4 ± 8.3	<0.001
Fins (uU/mL)	13.4 [8.3]	9 [4.3]	<0.001
HOMA-IR	3.1 [2.4]	1.8 [0.9]	<0.001
TG (mg/dL)	127.4 ± 62.6	78.5 ± 37.3	<0.001
AST (U/L)	23.8 ± 8.4	21.1 ± 6.8	0.002
ALT (U/L)	30.3 ± 14.5	21.4 ± 11.7	<0.001
AST/ALT	0.8 ± 0.2	1.1 ± 0.3	<0.001
Uric acid (mg/dL)	5.6 ± 1.3	4.7 ± 1.2	<0.001
Energy intake (kcal/d)	2501.8 ± 1011.5	2557.3 ± 1188.2	0.655

ALT, alanine transaminase; AST, aspartate transaminase; AST/ALT, AST to ALT ratio; BMI, body mass index; CRP, C-reactive protein; Fins, fasting insulin; FPG, fasting plasma glucose; HOMA-IR, homeostatic model assessment of insulin resistance; MetS, metabolic syndrome; PAL, physical activity level; TG, triacylglycerol.
Values given as mean ± standard deviation for parametric qualitative variables, median [interquartile range] for non-parametric variables and relative frequencies (%) for categorical variables.
*P-value: t test or Mann–Whitney P-value for quantitative and χ^2 P-value for categorical variables.

- The prudent pattern was a healthy diet consisting of oil-based cooked vegetables, legumes, potatoes, fruits, vegetables, and fatty fish.
- The high-protein pattern included red meat, poultry, and eggs.
- The unsaturated FA pattern included nuts, chocolate, and other foods rich in unsaturated FA.

These four factors explained 46% of the sample variability, with a KMO of 0.660 and Bartlett's test of sphericity <0.001. Factor loadings are presented in Table 2.

Mean scores for each dietary pattern of individuals with and without NAFLD are presented in Table 3. Overall, patients with NAFLD had a negative mean adherence score for the prudent, high-protein, and unsaturated FA dietary patterns and a positive score for the fast food pattern. The opposite direction was observed for controls. However, the difference of means between the groups was not statistically significant. Individuals in the fourth quartile of the fast food pattern had 3.9 times higher odds for NAFLD (95% confidence interval [CI], 1.571–9.682) than those in the first quartile, after adjusting for age, sex, energy intake, physical activity level (PAL), pack-years smoked, education years, and presence of MetS ($P = 0.003$; Table 4). Moreover, individuals in the second quartile of the unsaturated FA pattern had 55.7% reduced odds of developing the disease (95% CI, 0.205–0.961) than those in the first quartile, after adjusting for age, sex, energy intake, PAL, pack-years smoked, education years, and presence of MetS ($P = 0.039$). A higher consumption of this pattern was not associated with further protection from the disease.

A 1-unit increase in the fast food score was associated with 5% higher levels of C-reactive protein (CRP) and 0.294 mg/dL higher levels of uric acid, after adjusting for confounding factors ($P = 0.041$ and $P < 0.001$, respectively; Table 5). The score for the prudent pattern was negatively associated with TG and uric acid levels ($\beta = -5.960$; $P = 0.037$ and $\beta = -0.153$; $P = 0.035$, respectively). Greater adherence to the unsaturated FA pattern (per-unit increase) was statistically significantly associated with 6.1% and 6.4% lower levels of insulin and homeostatic model assessment of insulin resistance. The high-protein pattern was not associated with any NAFLD-related biomarker.

Discussion

In the present case-control study, four dietary patterns of 351 individuals with and without NAFLD were identified. We demonstrated associations between dietary patterns, NAFLD, and NAFLD-related biomarkers, independently of known confounding factors.

A greater adherence to a fast food–type dietary pattern was associated with higher odds for NAFLD. However, only individuals in the highest quartile compared with the lowest had a statistically significantly higher NAFLD risk, after adjusting for age, sex, energy intake, PAL, pack-years smoked, education years, and presence of MetS ($P = 0.003$). Individuals in the second quartile of the unsaturated FA pattern had a 55.7% reduced risk for developing the disease than those in the first quartile, after adjusting for the same confounding factors ($P = 0.039$). The fact that a higher adherence to the unsaturated FA pattern confers no additive effect compared with the lowest adherence may be explained by the fact that a greater intake of this pattern leads to an increased consumption of FA and energy overall. However, after adjusting for the other dietary patterns, only the fast food–type pattern association remained statistically significant. Over the past few years, published data

Table 2
Rotated factor-loading matrix for the four dietary patterns

	Dietary patterns			
Foods	Fast food type	Prudent	High protein	Unsaturated FA
Fast food main dishes	0.703	–	–	–
Sugar-sweetened soft drinks	0.655	–	–	–
Fried potatoes	0.644	–	–	–
Savory and puff pastry snacks	0.471	–	–	–
Olive oil–based cooked vegetables	–	0.745	–	–
Legumes	–	0.669	–	–
Potatoes	0.358	0.540	–	–
Fruits and vegetables	–	0.528	–	–
Fatty fish	–	0.510	–	–
Poultry	–	–	0.740	–
Eggs	–	–	0.682	–
Red meat	0.460	–	0.575	–
Nuts	–	–	–	0.654
Chocolate	–	–	–	0.604
Foods rich in unsaturated FA	–	–	–	0.595

FA, fatty acids.

Table 3
Mean *z*-scores of the four dietary patterns in NAFLD cases and controls

	Dietary patterns											
	Fast food type			Prudent			High protein			Unsaturated FA		
NAFLD	Mean	SD	*P*-value	Mean	SD	*P*-value	Mean	SD	*P*-value	Mean	SD	*P*-value
Cases	0.12	1.05	0.094	−0.06	1.03	0.376	−0.12	0.82	0.130	−0.03	1.07	0.628
Controls	−0.07	0.98		0.04	0.98		0.05	1.08		0.02	0.96	

NAFLD, non-alcoholic fatty liver disease; SD, standard deviation.

have supported that increased consumption of sugar-sweetened soft drinks, fructose, fat, and SFA constitute risk factors for NAFLD [16–19]. On the other hand, low fat intake, replacement of SFA by monounsaturated fatty acids (MUFA) and PUFA, and low-glycemic index foods favor liver health and reduce the risk for hepatic steatosis [20–24].

Only a few studies, to our knowledge, have focused on diet as a whole regarding NAFLD. In a Brazilian case-control study with elderly individuals, the regional snacks pattern, characterized by high carbohydrates and glycemic load, was independently associated with the disease (Prevalence ratio (PR) = 1.42, $P = 0.035$) [25]. Similarly, Jia et al. reported that in their population a high-carbohydrate or sweet dietary pattern was associated with higher prevalence of NAFLD in women only [8]. Moreover, in a Chinese study of 999 individuals, an animal food pattern was positively associated and a grains and vegetables pattern was inversely associated with the prevalence of NAFLD, and this association was independent of sex, age, PAL, body mass index, smoking status, and BP [10]. In the present study, an animal protein–based pattern was identified but not associated with disease risk. Recently, Fakhoury-Sayegh et al. reported that a high-fruit dietary pattern and a high-meat or fast food pattern constitute risk factors for NAFLD in Lebanese patients [26]. On the other hand, the traditional Lebanese diet consisting of vegetables and legumes was negatively associated with the odds of NAFLD. The fast food and the prudent dietary patterns of the present sample were similar to the high-meat or fast food and traditional Lebanese patterns of the Lebanese population, respectively.

A greater adherence to a Western-type diet, characterized by fried food, red and processed meat, high-fat foods, and high-sugar beverages, has been prospectively associated with NAFLD risk in adolescents [9]. Protective effects against hepatic steatosis and NAFLD severity have been attributed to the Mediterranean diet, with the main components of the diet being fiber, antioxidants, MUFA and PUFA [6,7,27]. The fast food pattern included most of the main components of the Western diet, whereas the prudent dietary pattern had a lot in common with the Mediterranean diet.

Moreover, dietary patterns consisting of high amounts of sugar, saturated, and trans-fatty acids have been strongly associated with all

Table 4
Association of quartiles of dietary patterns with NAFLD odds; results of multivariate binary logistic regressions

	Model 1*			Model 2†			Model 3‡			Model 4§		
Fast food type	OR	95% CI	*P*-value‖	OR	95% CI	*P*-value‖	OR	95% CI	*P*-value‖	OR	95% CI	*P*-value‖
Q1	Ref			Ref			Ref			Ref		
Q2	1.192	0.631–2.253	0.589	1.276	0.664–2.453	0.465	1.720	0.788–3.755	0.173	1.822	0.810–4.100	0.147
Q3	1.399	0.741–2.641	0.301	1.638	0.834–3.216	0.152	2.194	0.973–4.945	0.058	2.296	0.977–5.395	0.056
Q4	1.730	0.928–3.226	0.085	2.629	1.250–5.532	**0.011**	3.900	1.571–9.682	**0.003**	4.243	1.589–11.328	**0.004**
Prudent	OR	95% CI	*P*-value‖	OR	95% CI	*P*-value‖	OR	95% CI	*P*-value‖	OR	95% CI	*P*-value‖
Q1	Ref			Ref			Ref			Ref		
Q2	0.633	0.340–1.178	0.149	0.554	0.293–1.050	0.070	0.641	0.301–1.366	0.249	0.753	0.339–1.670	0.485
Q3	0.751	0.405–1.390	0.362	0.653	0.346–1.235	0.190	0.946	0.450–1.990	0.884	1.098	0.504–2.390	0.815
Q4	0.644	0.345–1.201	0.166	0.585	0.303–1.128	0.109	0.576	0.262–1.263	0.168	0.700	0.302–1.627	0.407
High protein	OR	95% CI	*P*-value‖	OR	95% CI	*P*-value‖	OR	95% CI	*P*-value‖	OR	95% CI	*P*-value‖
Q1	Ref			Ref			Ref			Ref		
Q2	1.188	0.647–2.181	0.579	1.239	0.664–2.314	0.501	1.528	0.724–3.227	0.266	1.856	0.837–4.120	0.128
Q3	0.581	0.306–1.102	0.096	0.630	0.326–1.218	0.169	0.662	0.301–1.457	0.305	0.685	0.302–1.553	0.365
Q4	0.912	0.489–1.699	0.771	1.094	0.555–2.157	0.795	1.450	0.645–3.262	0.368	1.677	0.716–3.931	0.234
Unsaturated FA	OR	95% CI	*P*-value‖	OR	95% CI	*P*-value‖	OR	95% CI	*P*-value‖	OR	95% CI	*P*-value‖
Q1	Ref			Ref			Ref					
Q2	0.662	0.354–1.239	0.197	0.565	0.296–1.078	0.083	0.443	0.205–0.961	**0.039**	0.497	0.224–1.102	0.085
Q3	0.987	0.536–1.819	0.968	0.862	1.622	0.646	0.949	0.451–1.996	0.889	1.135	0.524–2.457	0.749
Q4	0.686	0.366–1.286	0.240	0.618	1.187	0.148	0.647	0.299–1.400	0.269	0.824	0.367–1.850	0.640

CI, confidence interval; FA, fatty acids; MetS, metabolic syndrome; NAFLD, non-alcoholic fatty liver disease; OR, odds ratio; PAL, physical activity level.
*Model 1: Unadjusted.
†Model 2: Adjusted for age, sex, energy intake.
‡Model 3: Adjusted for age, sex, energy intake, PAL, pack-years smoked, education years, presence of MetS.
§Model 4: Adjusted for age, sex, energy intake, PAL, pack-years smoked, education years, presence of MetS, the other three dietary patterns.
‖Multivariate binary logistic regression *P*-value.
P-values ≤0.05 are in bold.

Table 5
Association of z-scores of dietary patterns with NAFLD-related biomarkers; results of multivariate linear regressions

		Fast food type			Prudent			High protein			Unsaturated FA		
		β	SE	*P*-value	β	SE	*P*-value	β	SE	*P*-value	β	SE	*P*-value
AST	Model 1*	−0.403	0.462	0.383	−0.167	0.426	0.696	0.358	0.445	0.421	−0.405	0.411	0.326
	Model 2†	−0.418	0.503	0.406	−0.263	0.449	0.559	0.151	0.483	0.755	−0.477	0.423	0.292
ALT	Model 1*	−0.165	0.803	0.838	0.335	0.740	0.651	−0.153	0.773	0.843	−1.038	0.713	0.147
	Model 2†	−0.567	0.875	0.517	0.057	0.780	0.942	−0.377	0.840	0.654	−1.099	0.736	0.136
AST/ALT	Model 1*	−0.014	0.019	0.445	$-2.269 * 10^{-5}$	0.017	0.999	−0.005	0.018	0.778	0.018	0.017	0.271
	Model 2†	−0.002	0.020	0.920	0.004	0.018	0.814	−0.005	0.019	0.779	0.020	0.017	0.238
TG	Model 1*	−2.877	3.032	0.343	−3.535	2.791	0.206	−1.573	2.932	0.592	−4.035	2.696	0.135
	Model 2†	−4.888	3.203	0.128	−5.960	2.843	**0.037**	−1.777	3.096	0.566	−5.211	2.678	0.053
FPG	Model 1*	0.196	0.631	0.756	0.576	0.581	0.322	−0.819	0.604	0.176	−0.711	0.562	0.207
	Model 2†	−0.058	0.635	0.927	0.176	0.566	0.756	−0.808	0.609	0.186	−0.742	0.535	0.166
LnFins	Model 1*	0.005	0.027	0.850	−0.047	0.025	0.058	0.011	0.026	0.659	−0.068	0.024	**0.004**
	Model 2†	0.021	0.027	0.420	−0.044	0.024	0.071	0.012	0.026	0655	−0.061	0.023	**0.008**
LnHOMA-IR	Model 1*	0.004	0.030	0.710	−0.040	0.027	0.147	0.001	0.028	0.963	−0.071	0.026	**0.007**
	Model 2†	0.025	0.029	0.379	−0.040	0.026	0.127	0.001	0.028	0.964	−0.064	0.025	**0.011**
LnCRP	Model 1*	0.048	0.025	0.063	0.002	0.023	0.927	−0.004	0.025	0.871	−0.001	0.023	0.970
	Model 2†	0.054	0.026	**0.041**	0.002	0.024	0.931	−0.002	0.026	0.937	−0.001	0.023	0.979
Uric acid	Model 1*	0.302	0.075	<**0.001**	−0.226	0.069	**0.001**	0.038	0.073	0.609	−0.133	0.068	0.053
	Model 2†	0.294	0.081	<**0.001**	−0.153	0.072	**0.035**	0.051	0.077	0.511	−0.090	0.069	0.193

ALT, alanine transaminase; AST, aspartate transaminase; AST/ALT, AST to ALT ratio; FA, fatty acids; FPG, fasting plasma glucose; LnFins, Ln(fasting insulin); LnHOMA-IR, Ln (homeostatic model assessment of insulin resistance); LnCRP, Ln(C-reactive protein); MetS, metabolic syndrome; PAL, physical activity level; TG, triacylglycerols.
*Model 1: Adjusted for age, sex, energy intake, presence of NAFLD.
†Model 2: Adjusted for age, sex, energy intake, presence of NAFLD, PAL, pack-years, education years, presence of MetS, and the other three dietary patterns.
‡ Multivariate binary logistic regression *P*-value.
P-values ≤0.05 are in bold.

the components of MetS [28–30]. Because NAFLD is now considered a possible extra feature of MetS, constituting its hepatic manifestation, we can assume that similar dietary patterns could affect risk for NAFLD. In line with this, Dietary Approaches to Stop Hypertension (DASH) diet, which is predominantly used for the treatment of hypertension, has been tested for its effect on NAFLD-related metabolic features [31]. The DASH diet is rich in fruits, vegetables, whole grains, fatty fish, low-fat dairy, and lean meat. Adherence to the DASH diet was found to significantly reduce alanine aminotransferase, TG, and alkaline phosphatase levels, markers of insulin metabolism and inflammation, whereas antioxidant markers were increased.

Based on the latter, we investigated the effect of the dietary patterns on disease- and metabolism-related biomarkers. Higher adherence to the fast food dietary pattern was independently associated with increased CRP and uric acid levels, whereas a higher adherence to the prudent pattern was independently associated with reduced TG and uric acid levels. CRP is a main indicator of systemic inflammation, and uric acid levels recently have been associated with risk for NAFLD [32,33]. TGs constitute one of the main triggers for NAFLD development [2]. The fast food–type pattern is rich in SFA and sugar, which have been shown to increase inflammation. Sugar-sweetened beverages are rich in fructose, and fast food main dishes are low in fiber and high in animal protein, which explains the increase in uric acid levels [34–36]. The prudent dietary pattern has a negative effect on TG levels because of its antioxidant properties. Moreover, it is low in animal protein and high in plant protein and fiber. These properties could explain the dietary pattern's protective effect against uric acid levels. Fruits also are included in the prudent pattern; however, it seems that a presumable increasing effect of fructose on uric acid levels is counteracted by an overall beneficial effect of the pattern. Moreover, higher adherence to the unsaturated FA pattern, a dietary pattern with strong antioxidant properties, was significantly associated with reduced insulin resistance and insulin levels.

To our knowledge, this is the first study to investigate the effect of different dietary patterns on NAFLD risk in a European population. Worldwide, there are only few studies in the field; therefore results of the present study could provide important contribution to the attempt of unraveling the role of the diet in NAFLD pathogenesis and treatment. Because NAFLD is a multifactorial disease, we adjusted the results for several known confounding factors. Moreover, we used a semiquantitative FFQ designed for the Greek community, which allowed for a better depiction of the dietary habits of the participants. Throughout the interview and assessment of each individual, we took all feasible actions to eliminate errors, misclassification, and recall bias.

The present study had some limitations that should be considered. First, because this was a case-control study, there was a risk for sampling and retrospective analysis bias. Moreover, we cannot claim that the dietary patterns are causative or protective for the disease because of the nature of this study. In addition, collection of dietary data through a FFQ has a great risk for overestimation of energy intake. Another important limitation is that analyzing a dietary data by PCA includes techniques that require subjectivity, such as grouping foods and choosing the number of factors. However, taking into account the aforementioned strengths and limitations, and the study design, we can conclude that the results of the present study could be generalized in individuals of Caucasian origin with similar lifestyle habits.

Conclusion

Patients with NAFLD were more adherent to a fast food–type dietary pattern than to a prudent, high-protein, or unsaturated FA diet. It can be concluded that following a fast food–type dietary pattern significantly increases the odds of NAFLD, but also increases CRP and uric acid levels. Moreover, higher consumption of a prudent diet, characterized by vegetables, fruits, legumes, fish, and olive oil, and a diet rich in unsaturated FAsreduces several NAFLD-related biomarkers. Nevertheless, larger case-control and prospective cohort studies are needed to replicate our results.

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