Arch Iran Med. March 2026;29(3):163-171

doi:10.34172/aim.35438

http://journalaim.com

ARCHIVES OF IRANIAN MEDICINE

Original Article

Open Access

Ultra-Processed Food Consumption and Its Association with Non-Alcoholic Fatty Liver Disease in Iranian Adults: A Case-Control Study

Mehdi Khakian[1,2], Sanaz Jamshidi[3], Mitra Kazemi Jahromi[4], Ebrahim Mokhtari[5,6], Setareh Alibakhshi[1,2], Niloufar Saber[7], Reza Sadeghi[1,2], Ammar Salehi-Sahlabadi[8,9], Elham Sobhrakhshankhah[10], Hossein Farhadnejad[5*], Farshad Teymoori[2*], Parvin Mirmiran[5]

[1]Nutritional Sciences Research Center, Iran University of Medical Sciences, Tehran, Iran
[2]Department of Nutrition, School of Public Health, Iran University of Medical Sciences, Tehran, Iran
[3]Center for Cohort Study of Shiraz University of Medical Sciences Employees, Shiraz University of Medical Sciences, Shiraz, Iran
[4]Endocrinology and Metabolism Research Center, Hormozgan University of Medical Sciences, BandarAbbas, Iran
[5]Nutrition and Endocrine Research Center, Research Institute for Endocrine Disorders, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[6]Department of Community Nutrition, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
[7]Faculty of Health, Southern Cross University, Gold Coast, Queensland, Australia
[8]Clinical Biochemistry Research Center, Basic Health Sciences Institute, Shahrekord University of Medical Sciences, Shahrekord, Iran
[9]Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, Iran
[10]Gastrointestinal and Liver Diseases Research Center, Iran University of Medical Sciences, Tehran, Iran

Abstract

Introduction: Non-alcoholic fatty liver disease (NAFLD) represents a rising global health challenge, marked by excessive fat deposition in the liver. The present case-control study sought to examine the relationship between intake of ultra-processed foods (UPFs) and the risk of NAFLD.

Methods: Out of 1000 invited individuals, this case-control study included 225 newly diagnosed NAFLD cases (confirmed via ultrasound) and 450 controls (aged 20–60 years) who underwent ultrasound screening to rule out hepatic steatosis. A validated food frequency questionnaire was used to assess dietary intake, and UPF consumption was quantified both as grams per day and as a percentage of total daily energy intake.

Results: The mean (SD) daily UPF consumption amounted to 147.5 (117.4) g, representing 15.4 (7.98)% of total energy intake. After adjusting for potential confounders, UPF intake (kcal/d) showed a positive association with odds of NAFLD (OR = 5.91; 95%CI: 2.96–11.78; *P* for trend < 0.001). A one-SD rise in UPF intake (SD = 221 kcal/d, roughly equivalent to 117.4 g/d of UPF) was linked to higher NAFLD odds (OR = 1.96; 95% CI: 1.63–2.41; *P* for trend < 0.001). When UPF intake was considered as a percentage of energy, the multivariable model revealed elevated NAFLD odds across tertiles (OR = 2.27; 95% CI: 1.26–4.10; *P* for trend < 0.001). In the fully adjusted model, each one-SD increment in UPF intake (SD = 7.98% of energy/day) was significantly associated with increased odds of NAFLD (OR = 1.29; 95%CI: 1.03–1.62; *P* for trend < 0.001).

Conclusion: A higher consumption of UPF may be related to increased odds of developing NAFLD.

Keywords: Adults, Dietary pattern, Non-alcoholic fatty liver disease, Ultra-processed foods

Cite this article as: Khakian M, Jamshidi S, Kazemi Jahromi M, Mokhtari E, Alibakhshi S, Saber N, et al. Ultra-Processed Food Consumption and Its Association with Non-Alcoholic Fatty Liver Disease in Iranian Adults: A Case-Control Study. Arch Iran Med 2026;29(3):163-171. doi:10.34172/aim.35438

Received: November 15, 2025, **Revised:** January 3, 2026, **Revised:** January 26, 2026, **Accepted:** April 18, 2026, **ePublished:** March 1, 2026

Introduction

Non-alcoholic fatty liver disease (NAFLD) ranks among the most common chronic disorders of the liver, with an estimated global prevalence of roughly 30% in adults, although considerable geographic differences exist.[1] The highest rates have been recorded in Latin America (44.4%), followed by the Middle East and North Africa (MENA) region (36.5%) and South Asia (33.8%).[2] According to meta-analyses conducted in Iran, approximately 33%–37% of the adult population is affected by NAFLD.[3,4] This considerable disease burden is largely driven by rising rates of obesity, type 2 diabetes, and sedentary behavior.[2,5]

Ultra-processed foods (UPFs) now make up a major part of modern dietary patterns and have been linked to a range of chronic metabolic diseases.[6] Diets high in UPFs typically contain more saturated fats, refined

*Corresponding Authors: Hossein Farhadnejad, Email: hosein.farhadnejad@gmail.com and Farshad Teymoori, Email: teymoori.f68@gmail.com

carbohydrates, and added sugars, and provide less fiber, leading to excess energy intake and metabolic disturbances.[7,8] In addition, UPFs may alter gut microbiota composition, promote intestinal dysbiosis and permeability, and consequently contribute to hepatic fat accumulation.[8,9] Higher consumption of UPFs has been also linked to insulin resistance, obesity, and metabolic syndrome, which are key risk factors for NAFLD.[7, 9-12]

Recent research has explored the relationship between UPF consumption and the likelihood of NAFLD.[13] Findings from Western and East Asian populations suggest that a higher intake of UPFs is associated with an elevated risk of NAFLD.[7,10-12,14,15] For instance, a study involving 143,073 participants from the UK Biobank cohort revealed that over a 10.5-year follow-up period, individuals in the highest quartile of UPF intake experienced a 26% higher risk of severe NAFLD (defined as hospitalization or death) relative to those in the lowest quartile.[15] In line with this, a US-based cohort study found that higher UPF consumption was associated with an 83% increase in the risk of NAFLD.[7] Additionally, the Tianjin cohort study reported that each 62.7 g/day increment in UPF consumption was associated with a 6% rise in the risk of NAFLD.[14] Furthermore, in obese adolescents, a high UPF intake was linked to a 2.3-fold increase in NAFLD odds, largely mediated by greater body fat.[16] In Korean obese youth, a 10% increase in UPF intake was linked to 37% higher odds of moderate-to-severe NAFLD.[17] Despite the growing global evidence, research on this topic remains limited in the MENA region, including Iran, where dietary patterns differ substantially from those of Western populations. A recent study among Iranian adults with type 2 diabetes found that higher UPF consumption was associated with greater odds of NAFLD.[18] However, data in the general Iranian population are lacking.

Considering the high prevalence of NAFLD and the increasing consumption of UPFs in Iran, this study aimed to examine the association between UPF intake and the likelihood of NAFLD in a sample of Iranian adults using a case–control design. The primary exposure metric in this study was UPF intake expressed as kcal/day. We selected this metric because it reflects the absolute energy contribution of UPFs to the diet and is commonly used in case-control studies of nutritional epidemiology, allowing direct comparison with previous literature. Additional measures comprised UPF consumption expressed as grams per day and as a proportion of total daily energy intake. Our pre-specified hypothesis was that a greater intake of UPFs (in kcal/day) would be linked to higher odds of NAFLD.

Materials and Methods

As illustrated in Figure 1, a total of 225 individuals with incident NAFLD and 450 healthy controls, all ranging between 20 and 60 years of age, were enrolled in this case-control investigation. The recruitment of participants took place at the Metabolic Liver Disease Research Center — a referral center affiliated with Isfahan University of Medical Sciences. All participants underwent abdominal ultrasonography using a GE Logiq S8 ultrasound system (GE Healthcare, USA) equipped with a convex transducer. Examinations were performed by an experienced

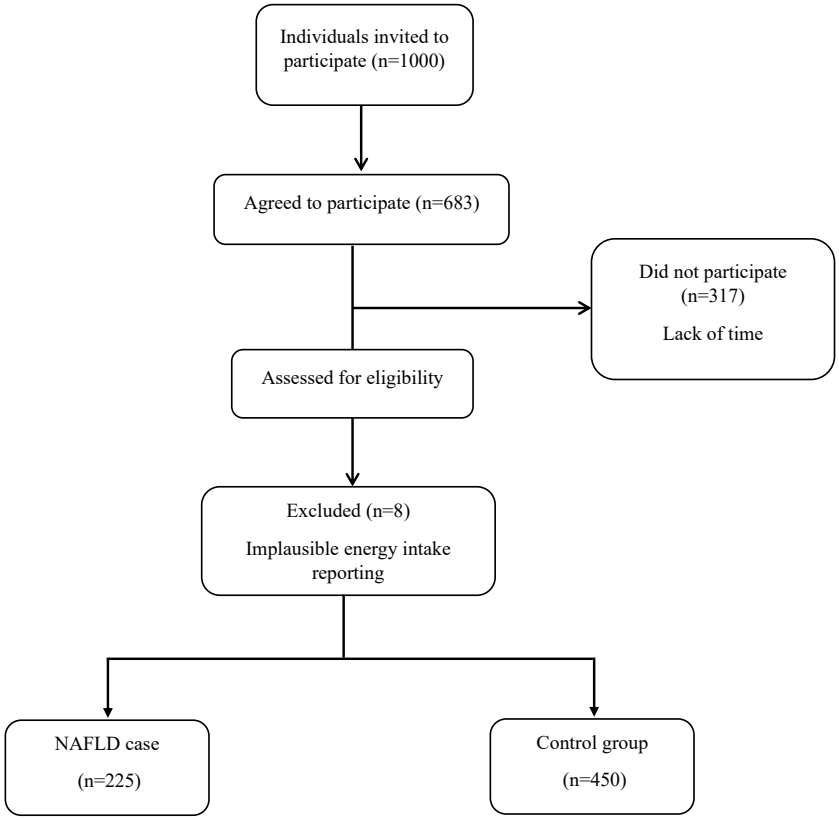

Figure 1. Schematic representation of participant recruitment and selection process in the present case-control study

radiologist in hepatobiliary imaging. The radiologist was blinded to participants' dietary intake data and other exposure variables related to the study hypothesis.

The diagnosis of hepatic steatosis was established using well-defined ultrasonographic criteria. These included: (a) a brighter echogenicity pattern in the liver relative to the renal cortex; (b) progressive weakening of the ultrasound beam as it passes through the liver; and (c) poor or incomplete visualization of the intrahepatic vessels as well as the diaphragm. Participants with ultrasonographic evidence of hepatic steatosis were classified as NAFLD cases, provided that other causes of liver disease and significant alcohol consumption had been excluded.

Cases and controls were clinic-based and were recruited through convenience sampling from individuals referred to the same center for routine abdominal, pelvic, or hepatobiliary ultrasonography. All individuals underwent the same standardized ultrasound protocol. Controls were eligible if they showed no ultrasonographic signs or clinical symptoms suggestive of NAFLD.

Exclusion criteria were as follows: (1) adherence to a specific diet; (2) history of chronic metabolic disorders (e.g. diabetes or thyroid dysfunction) or organ-specific diseases (e.g. kidney, cardiovascular, gastrointestinal, or hepatic diseases, including Wilson's disease, autoimmune hepatitis, hemochromatosis, viral hepatitis, and alcoholic fatty liver disease); (3) malignancy or autoimmune conditions; (4) use of hepatotoxic or steatogenic medications; (5) incomplete food frequency questionnaire (FFQ) data (< 35 items reported); and (6) implausible energy intakes (< 800 or > 4200 kcal/day) (8 participants). Because our goal was to recruit incident NAFLD cases, individuals with diabetes or other chronic metabolic disorders were excluded from both groups to minimize the likelihood of enrolling participants with long-standing NAFLD. This criterion, while necessary for identifying new cases, may limit generalizability to diabetic populations.

Dietary Assessment

To assess usual dietary intake over the preceding year, we employed a validated semi-quantitative food frequency questionnaire (FFQ) comprising 168 food items [19, 20]. This FFQ has been validated in the Iranian adult population and has demonstrated acceptable relative validity compared with repeated 24-hour dietary recalls, as well as good reproducibility over time. For each food item, participants indicated how often they consumed it using predefined frequency categories: "never," "monthly," "weekly," or "daily." The reported portion sizes were then transformed into grams using Iranian household measures.[21] Calculation of energy and nutrient intakes was performed primarily by referring to the United States Department of Agriculture (USDA) Food Composition Table (FCT)[22]; for traditional Iranian dishes not listed in the USDA database, the Iranian FCT was used as the source of nutritional data.[23] Finally, all frequency reports were converted to average daily intake expressed as grams per day.

Ultra-processed Food (UPF) Classification

UPF consumption was identified and quantified based on the NOVA classification system.[24] The classification of food items was guided by the NOVA food-group definitions and examples provided in the supplementary material of the reference study.[24] All FFQ items were matched to the corresponding NOVA categories using this published framework. The following food groups were classified as UPFs (NOVA group 4): cereals-based processed foods (cakes, biscuits, crackers, baguettes, toast, pasta, noodles, and pizza); confectionery and sweetened products (candies, sweets, chocolates, jam, caramel cream, and ice cream); processed meats (hamburgers, sausages, and other burgers); fried and savory snacks (fried potatoes, potato chips, and puffs); dairy-based processed items (creamy cheese, skim milk, cocoa milk, and chocolate milk); condiments and sauces (mayonnaise, margarine, hydrogenated fats, and tomato sauce); and sugar-sweetened beverages (carbonated soft drinks and canned juices). For each participant, UPF intake was calculated in three ways: (1) absolute UPF intake (g/day), obtained by summing the gram amounts of all FFQ items classified as UPFs; (2) total energy intake from UPFs (kcal/day), calculated by summing the caloric contribution of all UPF items; and (3) the percentage contribution of UPFs to total daily energy intake, calculated as (UPF kcal/day ÷ total daily kcal/day) × 100.

Assessment of Other Variables

A standardized questionnaire was employed to gather sociodemographic information, which included age, sex, medical history, medication use (categorized as yes or no), smoking status (yes/no), and socioeconomic status (SES) classified into three levels: low, moderate, and high.[25] Physical activity levels were evaluated via in-person interviews using the International Physical Activity Questionnaire (IPAQ),[26] and the resulting data were expressed as metabolic equivalents per week (METs/week).[27,28] The full details of our measurement protocols, coding of variables, and categorization methods have been already described extensively in one of our earlier publications.[29] Body weight was recorded with a calibrated digital scale (Seca 707, Hamburg, Germany) to the nearest 0.1 kg, while participants wore lightweight clothing and no shoes. Height was measured to the nearest 0.5 cm using a portable stadiometer (Seca 208). Thereafter, body mass index (BMI) was derived by dividing weight (in kilograms) by the square of height (in meters).

Statistical Analysis

Statistical analyses were carried out using IBM SPSS Statistics, version 21.0. To determine whether continuous variables followed a normal distribution, we applied the Kolmogorov–Smirnov test and also examined the histograms visually. Continuous data are summarized either as mean along with standard deviation (SD) or

as median accompanied by interquartile range (IQR), depending on their distribution. Categorical variables are reported as percentages. For between-group comparisons, normally distributed continuous variables were analyzed using independent-samples *t*-tests, whereas categorical variables were compared by means of Chi-square tests.

UPF intake was operationalized using two complementary energy-based metrics, absolute UPF energy intake (kcal/day) and the proportion of total energy derived from UPF (% of total energy), defined *a priori* to capture both total metabolic exposure and the relative dietary contribution of UPF. Participants were divided into tertiles according to their level of UPF intake. To examine trends across these tertiles, linear regression was applied for continuous variables, whereas Chi-square tests were used for categorical ones. We employed multivariable logistic regression models to calculate odds ratios (ORs) along with their corresponding 95% confidence intervals (CIs) for NAFLD across tertiles. The crude model was unadjusted. Model 1 was adjusted for age and sex, and Model 2 was further adjusted for BMI, smoking status, physical activity, SES, and total energy intake. For all statistical tests, a two-sided *P*-value of less than 0.05 was considered to indicate statistical significance.

Results

In the overall study sample, the average age was 38.1 years (SD = 8.85), and the mean body mass index (BMI) was 26.8 kg/m² (SD = 4.31). The mean (SD) daily intake of UPFs was 147.5 (117.4) g/day, which provided 325 (221) kcal/day, corresponding to 15.4% (7.98%) of total energy intake. These SD values were used for estimating "per-SD" odds ratios**.** In the case and control groups, the mean (SD) ages were 37.8 (8.91) and 38.6 (8.71) years, respectively, and the mean (SD) BMIs were 30.5 (4.02) and 25.0 (3.09) kg/m².

Table 1 presents the characteristics of participants across tertiles of UPF intake. Mean age and the proportion of smokers increased with higher UPF intake. Similarly, mean fat intake (% of total energy), absolute UPF intake (g/day), UPF contribution to total energy (%), and calories from UPFs all increased across tertiles ($P<0.05$). In contrast, carbohydrate and protein intake (% of total energy) decreased with increasing UPF consumption ($P<0.05$). There was no differences across tertiles for other variables, including sex distribution, BMI, physical activity, educational level, SES, or total daily energy intake.

Comparisons between case and control groups are reported in Table 2. Participants with NAFLD had higher mean BMI, daily energy intake, UPF consumption, and smoking prevalence compared with controls ($P<0.05$). Conversely, physical activity levels and the proportion of individuals with high SES were lower in the case group ($P<0.05$). There were no differences for age, sex distribution, educational level, or macronutrient intake (carbohydrates, protein, and fat) between cases and controls.

The (ORs) along with their 95% (CIs) for NAFLD, categorized by tertiles of absolute UPF intake (kcal/d) and by the proportion of total energy derived from UPFs, are displayed in Table 3.After adjustment for age and sex, individuals in higher tertiles of UPF intake (kcal/d) showed greater odds of NAFLD, with an OR of 4.64 (95%

Table 1. Participant characteristics by tertile categories of ultra-processed food intake

Variables	Tertiles of UPFs (% of energy)			*P*-trend
	T_1 (*n* = 195)	T_2 (*n* = 238)	T_3 (*n* = 242)	
Demographic data				
Age, (year)	39.1 ± 9.43	38.4 ± 9.02	37.0 ± 8.10	0.018
Sex (male)	50.3	53.8	54.5	0.644
Body mass index (kg/m²)	26.5 ± 4.01	26.7 ± 4.52	27.0 ± 4.33	0.102
Physical activity (MET/h/week)	1355 ± 803	1532 ± 971	1398 ± 841	0.917
Smoking (yes)	2.6	2.5	7.0	0.024
Education level (Bachelor and higher, %)	47.2	46.2	52.9	0.974
Socio economic status				0.508
Low	29.2	24.8	30.6	
Middle	39.5	40.8	34.7	
High	31.3	34.5	34.7	
Dietary intake				
Energy intake (Kcal/d)	2217 ± 625	2173 ± 582	2264 ± 656	0.303
Carbohydrate (% Kcal)	56.7 ± 7.33	56.7 ± 6.42	54.5 ± 6.65	< 0.001
Protein (% Kcal)	13.4 ± 2.70	13.2 ± 2.14	13.1 ± 2.07	0.191
Fat (% Kcal)	29.8 ± 7.14	30.0 ± 6.49	32.3 ± 6.71	< 0.001
UPF (g/d)	70.4 ± 41.2	125.7 ± 54.8	231.2 ± 148.1	< 0.001
UPF (Kcal/d)	150.4 ± 65.8	275.8 ± 82.9	514.8 ± 252.8	< 0.001
UPF (percent of energy/d)	7.30 ± 2.14	13.5 ± 1.79	23.9 ± 6.40	< 0.001

UPF; Ultra-processed foods. Continuous variables are presented as mean (SD), whereas categorical variables are reported as percentages (%)

CI: 2.93–7.33; *P* for trend < 0.001). In the fully adjusted multivariable model, adjusted for age, sex, BMI, smoking status, physical activity, SES, and total energy intake, the positive association between UPF consumption (kcal/d) and NAFLD became even stronger, yielding an OR of 5.91 (95% CI: 2.96–11.78; *P* for trend < 0.001). Furthermore, each increment of one SD in UPF intake (kcal/d) was associated with elevated odds of NAFLD (OR = 1.96; 95% CI: 1.63–2.41; *P* for trend < 0.001).

When UPF intake was considered as a percentage of total energy intake, the model adjusting for age and sex revealed an increase in the odds of NAFLD across rising tertiles (OR = 2.08; 95% CI: 1.36–3.19; P for trend = 0.003). After additional adjustment for multiple covariates in the multivariable model, the positive association remained statistically significant (OR = 2.27; 95% CI: 1.26–4.10; P for trend < 0.001). Finally, in the fully adjusted model, each one-SD increment in UPF intake (expressed as percentage of energy per day) was significantly related to higher odds of NAFLD (OR = 1.29; 95% CI: 1.03–1.62; *P* for trend < 0.001).

Table 2. Characteristics of the study population according to case and control status

Variables	Non-NAFLD (*n* = 450)	NAFLD (*n* = 225)	*P* value*
Demographic data			
Age, (year)	37.9 ± 8.9	38.6 ± 8.7	0.296
Sex (male)	51.8	55.6	0.354
Body mass index (kg/m²)	25.0 ± 3.0	30.5 ± 4.0	< 0.001
Physical activity (MET/min/week)	1590 ± 949	1119 ± 616	< 0.001
Smoking (yes)	2.7	7.1	0.006
Education level (Bachelor and higher, %)	47.8	44.9	0.478
Socio economic status			
Low	31.6	21.3	
Middle	40.4	33.8	< 0.001
High	28	44.9	
Dietary intake			
Energy intake (Kcal/d)	2170 ± 625	2315 ± 606	0.004
Carbohydrate (% Kcal)	55.9 ± 6.5	55.9 ± 7.4	0.913
Fat (% Kcal)	30.83 ± 6.54	30.8 ± 7.4	0.939
Protein (% Kcal)	13.2 ± 2.2	13.2 ± 2.4	0.924
UPF (g/d)	120.1 ± 82.8	202.4 ± 152.4	< 0.001
UPF (Kcal/d)	279.1 ± 176.5	417.6 ± 269.2	< 0.001
UPF (percent of energy/d)	14.5 ± 7.55	17.2 ± 8.51	< 0.001

UPF; Ultra-processed foods.
Continuous and categorical variables are presented as mean ± SD and percentage (%), respectively.
**P* values were calculated by means of the independent-samples *t*-test (for continuous variables) and the Chi-square test (for categorical variables).

Discussion

In this case-control study, after controlling for potential confounders, including age, sex, BMI, smoking, physical activity, SES, and total energy intake, a high level of UPF consumption was observed to be possibly associated with higher odds of NAFLD in Iranian adults.

As BMI may occupy an intermediate position in the causal relationship between UPF intake and NAFLD, adjusting for this variable could lead to overadjustment bias. Therefore, we presented models both with and without BMI. The persistence of significant associations across all models, together with the slightly stronger estimates after BMI adjustment, suggests that BMI may not fully mediate the relationship but may also confound part of the association. Interpretation of BMI-adjusted estimates should therefore be made with caution. Notably, the stronger association observed after adjustment for BMI may reflect a suppression (negative confounding) effect, whereby BMI partially masked the true relationship between UPF intake and NAFLD in the age- and sex-adjusted model.

Our findings indicate that individuals with NAFLD tend to follow less healthy lifestyle patterns. As a

Table 3. Odds ratios (95% CI) for non-alcoholic fatty liver disease according to UPF tertiles and per one-SD increase in UPF consumption

Dietary indices	OR (95% CI) of NAFLD					
	Tertile 1	Tertile 2	Tertile 3	P trend*	Per one SD	*P* Value
UPF (Kcal/d)						
Median score	130.0	243.0	428.0		221.0	
Cases (n = 225) / Controls (n = 450)	30 / 150	56 / 149	139 / 151			
Crude model	1.00 (Ref)	1.87 (1.14 – 3.09)	4.60 (2.92 – 7.25)	< 0.001	1.97 (1.62 – 2.39)	< 0.001
Model 1*	1.00 (Ref)	1.88 (1.14 – 3.10)	4.64 (2.93 – 7.33)	< 0.001	1.98 (1.63 – 2.41)	< 0.001
Model 2†	1.00 (Ref)	2.57 (1.29 – 5.13)	5.91 (2.96 – 11.78)	< 0.001	1.96 (1.63 – 2.41)	< 0.001
UPF (Percentage of energy/d)						
Median score	7.6	13.6	22.6		7.98	
Cases (n = 225) / Controls (n = 450)	45 / 150	88 / 150	92 / 150			
Crude model	1.00 (Ref)	1.95 (1.27 – 2.99)	2.04 (1.34 – 3.11)	0.003	1.38 (1.17 – 1.62)	< 0.001
Model 1*	1.00 (Ref)	1.96 (1.28 – 3.00)	2.08 (1.36 – 3.19)	0.002	1.39 (1.18 – 1.63)	< 0.001
Model 2†	1.00 (Ref)	1.89 (1.05 – 3.38)	2.27 (1.26 – 4.10)	< 0.001	1.29 (1.03 – 1.62)	< 0.001

UPF; Ultra-processed foods.
*Model 1: adjusted for age and sex
† Model 2: adjusted for model 1 and body mass index, smoking, physical activity, socio-economic status, and dietary intake of energy

multifactorial disease, NAFLD is influenced by dietary habits and lifestyle choices.[30] In recent decades, global lifestyle changes, including increased consumption of calorie-dense foods, higher rates of smoking, and reduced physical activity, have contributed to a rising prevalence of metabolic disorders.[30,31] NAFLD is also closely linked to obesity, with longitudinal studies demonstrating that weight gain over the life course significantly increases the risk of developing NAFLD.[32,33]

Consistent with previous research, participants with NAFLD in our study reported poor dietary habits. According to the findings of Bashir *et al*., among individuals with NAFLD, over 65% reported a high intake of fried foods, fast foods, and sugar-sweetened beverages; conversely, their consumption of fruits and vegetables was inadequate, and they engaged in limited regular physical activity.[34] Another study reported an inverse relationship between NAFLD and adherence to healthy dietary patterns, alongside a direct association with consumption of regional snacks.[35] In non-obese individuals, Kwak *et al*. identified low carbohydrate intake and insufficient physical activity as independent predictors of NAFLD.[36] Furthermore, a meta-analysis confirmed the association observed between smoking and NAFLD, potentially mediated through changes in body fat distribution, oxidative glucose metabolism, elevated plasma free fatty acids, and insulin resistance.[37] Socioeconomic status also appears to influence NAFLD risk, as shown in Iranian and Korean populations.[38,39]

Given the high prevalence of NAFLD and the limited availability of targeted treatments, dietary quality has become a key focus for disease prevention and management. Our results support this perspective, demonstrating that higher UPF intake is related to greater odds of NAFLD. Zhao *et al*. reported similar findings, linking UPF consumption to NAFLD risk in both adolescents and adults, primarily through increased body fat.[16] Song *et al*. highlighted the harmful effects of UPFs on liver health, particularly in promoting steatosis, although their relationship with fibrosis remains less clear.[40] Findings from a prospective cohort study conducted in the UK further revealed a direct relationship between higher consumption of UPF and an elevated risk of NAFLD.[15]

Several mechanisms may underlie these associations. UPFs can induce intestinal dysbiosis by promoting the growth of pro-inflammatory microorganisms, while additives and packaging chemicals, such as monosodium glutamate, bisphenol A, and artificial sweeteners, can disrupt the gut microbiome, impair the intestinal mucus barrier, and trigger systemic inflammation via the gut–liver axis.[41-43] Endocrine disruptors, including dioxins, bisphenol A, and phthalates, may further contribute to hepatic insulin resistance and NAFLD development.[44] From a nutritional standpoint, UPFs are generally characterized by high energy density, elevated levels of added sugars and saturated fats, as well as insufficient amounts of dietary fiber, protein, several micronutrients (including potassium, zinc, and magnesium), and various vitamins (such as A, C, D, E, B12, and niacin). These dietary features are, in turn, associated with obesity and type 2 diabetes—both of which are well-established major risk factors for NAFLD.[45-48] In addition, UPFs are rich in advanced glycation end products (AGEs) due to high sugar, fructose, and fat content, as well as industrial high-temperature cooking methods, which may promote NAFLD.[11,49] According to Quetglas-Llabrés *et al*., individuals with metabolic syndrome who have high UPF intake display a more pro-oxidant and inflammatory state, which probably stems from AGE formation.[50,51]

To the best of our knowledge, this investigation represents the first assessment of the relationship between UPF consumption and NAFLD odds among the general adult population of Iran. Key strengths of the present work are a substantial sample size, application of a validated FFQ, and enrollment of both cases and controls from a single center to enhance comparability. We also adjusted for multiple potential confounders to reduce bias. However, several limitations should be acknowledged. First, because of the case-control nature of the present work, causal relationships cannot be established. Reverse causation, where the presence of disease influences dietary recall or habits, is a potential concern in case-control studies; however, because we included only incident NAFLD cases (newly diagnosed), the possibility of reverse causation (i.e. dietary changes due to pre-existing disease) is substantially reduced. Second, selection bias may have been introduced, as controls were recruited from the same clinical setting. Third, use of an FFQ for dietary assessment introduces the potential for recall bias and measurement error, as it relies on participants' long-term memory. Although we cannot completely eliminate this issue, we used a validated FFQ to minimize this limitation. Fourth, outcome misclassification is another potential limitation. Although ultrasound is a widely accepted tool for NAFLD diagnosis, it has imperfect sensitivity, particularly for mild hepatic steatosis. Consequently, some individuals with mild NAFLD may have been misclassified as controls (non-differential misclassification). This type of misclassification typically biases the association toward the null, meaning that the true odds ratio between UPF intake and NAFLD is likely stronger than what we observed.

Fifth, the generalizability of our findings is subject to limitation. This study was conducted at a single referral center in Iran, which may limit the representativeness of the sample to the general population. Referral and selection biases may exist, as individuals referred to this center may differ from those in other healthcare settings or the general population. However, use of a referral center strengthens internal validity by ensuring standardized diagnostic procedures and reducing heterogeneity. Additionally, we excluded individuals with certain comorbidities (e.g. viral hepatitis, alcoholic liver disease, other chronic liver diseases) to reduce confounding. Although this exclusion enhances internal validity, it might limit the applicability

of our findings to NAFLD patients presenting with such comorbidities. Hence, caution is warranted when extrapolating our results to other populations or clinical contexts.

Conclusion

In conclusion, our findings suggest that a dietary pattern high in UPFs may be linked to a higher likelihood of NAFLD in Iranian adults, independent of major confounders. The present findings should be regarded as associative rather than causal; consequently, additional prospective cohort investigations are required to verify this relationship and to clarify the biological mechanisms that underlie it.

Acknowledgments

The authors acknowledge Isfahan University of Medical Sciences and Iran University of Medical Sciences for their cooperation and support. Appreciation is also extended to all individuals who participated in the study for their invaluable input.

Authors' Contribution

Conceptualization: Mehdi Khakian, Mitra Kazemi Jahromi, Farshad Teymoori, Parvin Mirmiran
Data curation: Setareh Alibakhshi, Niloufar Saber, Reza Sadeghi
Formal Analysis: Mehdi Khakian, Setareh Alibakhshi, Ammar Salehi-sahlabadi, Farshad Teymoori
Investigation: Farshad Teymoori
Methodology: Farshad Teymoori, Mehdi Khakian
Project administration: Hossein Farhadnejad, Farshad Teymoori
Resources: Hossein Farhadnejad, Farshad Teymoori
Software: Farshad Teymoori
Supervision: Hossein Farhadnejad, Farshad Teymoori
Validation: Hossein Farhadnejad
Visualization: Hossein Farhadnejad
Writing – original draft: Mehdi Khakian, Sanaz Jamshidi, Ebrahim Mokhtari, Elham Sobhrakhshankhah
Writing – review & editing: Mehdi Khakian, Sanaz Jamshidi, Niloufar Saber, Reza Sadeghi, Hossein Farhadnejad, Farshad Teymoori

Competing Interests

The authors declare the is no conflict of interest.

Data Availability Statement

The data sets examined in this investigation can be obtained from the corresponding author upon reasonable request.

Consent for Publication

Not applicable

Ethical Approval and Consent to Participate

Written informed consent was secured from all individuals enrolled. All human participant procedures in this study conformed to the ethical guidelines of the relevant institutional and national research committee as well as the 1964 Helsinki Declaration (including its subsequent amendments) or equivalent ethical standards. Approval for the study was granted by the Ethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran.

Funding

No funding.

References

1. Teng ML, Ng CH, Huang DQ, Chan KE, Tan DJ, Lim WH, et al. Global incidence and prevalence of nonalcoholic fatty liver disease. Clin Mol Hepatol 2023;29(Suppl):S32-42. doi:10.3350/cmh.2022.0365
2. Younossi ZM, Golabi P, Paik JM, Henry A, Van Dongen C, Henry L. The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): a systematic review. Hepatology 2023;77(4):1335-47. doi:10.1097/hep.0000000000000004
3. Tabaeian SP, Rezapour A, Azari S, Martini M, Saran M, Behzadifar M, et al. Prevalence of non-alcoholic fatty liver disease in Iran: a systematic review and meta-analysis. J Clin Exp Hepatol 2024;14(1):101209. doi:10.1016/j.jceh.2023.06.009
4. Hassanipour S, Amini-Salehi E, Joukar F, Khosousi MJ, Pourtaghi F, Ansar MM, et al. The prevalence of non-alcoholic fatty liver disease in Iranian children and adult population: a systematic review and meta-analysis. Iran J Public Health 2023;52(8):1600-12. doi:10.18502/ijph.v52i8.13399
5. Wong VW, Ekstedt M, Wong GL, Hagström H. Changing epidemiology, global trends and implications for outcomes of NAFLD. J Hepatol 2023;79(3):842-52. doi:10.1016/j.jhep.2023.04.036
6. Elizabeth L, Machado P, Zinöcker M, Baker P, Lawrence M. Ultra-processed foods and health outcomes: a narrative review. Nutrients 2020;12(7):1955. doi:10.3390/nu12071955
7. Liu Z, Huang H, Zeng Y, Chen Y, Xu C. Association between ultra-processed foods consumption and risk of non-alcoholic fatty liver disease: a population-based analysis of NHANES 2011-2018. Br J Nutr 2023;130(6):996-1004. doi:10.1017/s0007114522003956
8. Hägele FA, Enderle J, Rimbach G, Bosy-Westphal A. Ultra-processed food consumption and the risk of non-alcoholic fatty liver disease—what are the proposed mechanisms? Explor Dig Dis 2023;2(4):133-48. doi:10.37349/edd.2023.00023
9. Shi L, Li Z, Ma X, Wang J, Wu Y, Zhu Y, et al. Effects of ultra-processed foods on the liver: insights from gut microbiome and metabolomics studies in rats. Front Nutr 2024;11:1503879. doi:10.3389/fnut.2024.1503879
10. Henney AE, Gillespie CS, Alam U, Hydes TJ, Cuthbertson DJ. Ultra-processed food intake is associated with non-alcoholic fatty liver disease in adults: a systematic review and meta-analysis. Nutrients 2023;15(10):2266. doi:10.3390/nu15102266
11. Grinshpan LS, Eilat-Adar S, Ivancovsky-Wajcman D, Kariv R, Gillon-Keren M, Zelber-Sagi S. Ultra-processed food consumption and non-alcoholic fatty liver disease, metabolic syndrome and insulin resistance: a systematic review. JHEP Rep 2024;6(1):100964. doi:10.1016/j.jhepr.2023.100964
12. Konieczna J, Fiol M, Colom A, Martínez-González M, Salas-Salvadó J, Corella D, et al. Does consumption of ultra-processed foods matter for liver health? Prospective analysis among older adults with metabolic syndrome. Nutrients 2022;14(19):4142. doi:10.3390/nu14194142
13. Zhang J, Shu L, Chen X. Ultra-processed foods and non-alcoholic fatty liver disease: an updated systematic review and dose-response meta-analysis. Front Nutr 2025;12:1631975. doi:10.3389/fnut.2025.1631975
14. Zhang S, Gan S, Zhang Q, Liu L, Meng G, Yao Z, et al. Ultra-processed food consumption and the risk of non-alcoholic fatty liver disease in the Tianjin Chronic Low-Grade Systemic Inflammation and Health Cohort Study. Int J Epidemiol 2022;51(1):237-49. doi:10.1093/ije/dyab174
15. Zhang YF, Qiao W, Zhuang J, Feng H, Zhang Z, Zhang Y. Association of ultra-processed food intake with severe non-alcoholic fatty liver disease: a prospective study of 143073 UK Biobank participants. J Nutr Health Aging 2024;28(10):100352. doi:10.1016/j.jnha.2024.100352
16. Zhao L, Zhang X, Martinez Steele E, Lo CH, Zhang FF, Zhang X. Higher ultra-processed food intake was positively associated with odds of NAFLD in both US adolescents and adults: a national survey. Hepatol Commun 2023;7(9):e0240.

doi:10.1097/hc9.0000000000000240
17. Lee GY, Lim JH, Joung H, Yoon D. Association between ultra-processed food consumption and metabolic disorders in children and adolescents with obesity. Nutrients 2024;16(20):3524. doi:10.3390/nu16203524
18. Alikhani A, Seraj A, Kakoienejad MH, Poustchi H, Yari Z. Associations between ultra-processed foods and risk of non-alcoholic fatty liver disease in patients with type 2 diabetes: a cross-sectional study. Iran J Nutr Sci Food Technol 2025;20(1):13-21. doi:10.61186/nsft.20.1.13
19. Hosseini-Esfahani F, Asghari G, Mirmiran P, Azizi F. Reproducibility and relative validity of food group intake in a food frequency questionnaire developed for the Tehran Lipid and Glucose Study. J Epidemiol 2010;20(2):150-8. doi:10.2188/jea.je20090083
20. Asghari G, Rezazadeh A, Hosseini-Esfahani F, Mehrabi Y, Mirmiran P, Azizi F. Reliability, comparative validity and stability of dietary patterns derived from an FFQ in the Tehran Lipid and Glucose Study. Br J Nutr 2012;108(6):1109-17. doi:10.1017/s0007114511006313
21. Ghaffarpour M, Houshiar-Rad A, Kianfar HJ. The Manual for Household Measures, Cooking Yields Factors and Edible Portion of Foods. Tehran: Nashre Olume Keshavarzy; 1999. p. 42-58.
22. Bowman SA, Friday JE, Moshfegh AJ. MyPyramid Equivalents Database, 2.0 for USDA Survey Foods, 2003-2004: Documentation and User Guide. US Department of Agriculture; 2008. Available from: http://www.ars.usda.gov/ba/bhnrc/fsrg.
23. Azar M, Sarkisian E. Food composition table of Iran. Vol 65. Tehran: National Nutrition and Food Research Institute, Shaheed Beheshti University; 1980. p. 12.
24. Monteiro CA, Cannon G, Levy RB, Moubarac JC, Louzada ML, Rauber F, et al. Ultra-processed foods: what they are and how to identify them. Public Health Nutr 2019;22(5):936-41. doi:10.1017/s1368980018003762
25. Garmaroudi GR, Moradi A. Socio-economic status in Iran: a study of measurement index. Payesh 2010;9(2):137-44.
26. Baghiani Moghaddam MH, Bakhtari Aghdam F, Asghari Jafarabadi M, Allahverdipour H, Dabagh Nikookheslat S, Safarpour S. The Iranian version of International Physical Activity Questionnaire (IPAQ) in Iran: content and construct validity, factor structure, internal consistency and stability. World Appl Sci J 2012;18(8):1073-80. doi:10.5829/idosi.wasj.2012.18.08.754
27. Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, et al. Compendium of physical activities: an update of activity codes and MET intensities. Med Sci Sports Exerc 2000;32(9 Suppl):S498-504. doi:10.1097/00005768-200009001-00009
28. Lee PH, Macfarlane DJ, Lam TH, Stewart SM. Validity of the International Physical Activity Questionnaire Short Form (IPAQ-SF): a systematic review. Int J Behav Nutr Phys Act 2011;8:115. doi:10.1186/1479-5868-8-115
29. Kazemi Jahromi M, Saber N, Norouzzadeh M, Daftari G, Pourhabibi-Zarandi F, Ahmadirad H, et al. Carbohydrate quality index and risk of non-alcoholic fatty liver disease in Iranian adults. BMC Endocr Disord 2024;24(1):195. doi:10.1186/s12902-024-01609-1
30. Nseir W, Hellou E, Assy N. Role of diet and lifestyle changes in nonalcoholic fatty liver disease. World J Gastroenterol 2014;20(28):9338-44. doi:10.3748/wjg.v20.i28.9338
31. Wu W, Ma W, Yuan S, Feng A, Li L, Zheng H, et al. Associations of unhealthy lifestyle and nonalcoholic fatty liver disease with cardiovascular healthy outcomes. J Am Heart Assoc 2023;12(23):e031440. doi:10.1161/JAHA.123.03144
32. Rojano A, Sena E, Manzano-Nuñez R, Pericàs JM, Ciudin A. NAFLD as the metabolic hallmark of obesity. Intern Emerg Med 2023;18(1):31-41. doi:10.1007/s11739-022-03139-x
33. Kim MN, Lo CH, Corey KE, Liu PH, Ma W, Zhang X, et al. Weight gain during early adulthood, trajectory of body shape and the risk of nonalcoholic fatty liver disease: a prospective cohort study among women. Metabolism 2020;113:154398. doi:10.1016/j.metabol.2020.154398
34. Bashir Y, Rashid S. Association between lifestyle factors and fatty liver disease among young adults in Islamabad. Journal of Political Stability Archive 2025;3(1):389-403.
35. Adriano LS, de Carvalho Sampaio HA, Arruda SP, de Melo Portela CL, de Melo ML, Carioca AA, et al. Healthy dietary pattern is inversely associated with non-alcoholic fatty liver disease in elderly. Br J Nutr 2016;115(12):2189-95. doi:10.1017/s0007114516001410
36. Kwak JH, Jun DW, Lee SM, Cho YK, Lee KN, Lee HL, et al. Lifestyle predictors of obese and non-obese patients with nonalcoholic fatty liver disease: a cross-sectional study. Clin Nutr 2018;37(5):1550-7. doi:10.1016/j.clnu.2017.08.018
37. Akhavan Rezayat A, Dadgar Moghadam M, Ghasemi Nour M, Shirazinia M, Ghodsi H, Rouhbakhsh Zahmatkesh MR, et al. Association between smoking and non-alcoholic fatty liver disease: a systematic review and meta-analysis. SAGE Open Med 2018;6:2050312117745223. doi:10.1177/2050312117745223
38. Sadeghianpour Z, Cheraghian B, Farshchi HR, Asadi-Lari M. Non-alcoholic fatty liver disease and socioeconomic determinants in an Iranian cohort study. BMC Gastroenterol 2023;23(1):350. doi:10.1186/s12876-023-02964-4
39. Cho J, Lee I, Park DH, Kwak HB, Min K. Relationships between socioeconomic status, handgrip strength, and non-alcoholic fatty liver disease in middle-aged adults. Int J Environ Res Public Health 2021;18(4):1892. doi:10.3390/ijerph18041892
40. Song J, Chen S, Qian K, Ye W. Association of ultra-processed foods consumption with increased liver steatosis in US adults. Front Nutr 2025;12:1536989. doi:10.3389/fnut.2025.1536989
41. García S, Monserrat-Mesquida M, Ugarriza L, Casares M, Gómez C, Mateos D, et al. Ultra-processed food consumption and metabolic-dysfunction-associated steatotic liver disease (MASLD): a longitudinal and sustainable analysis. Nutrients 2025;17(3):472. doi:10.3390/nu17030472
42. Liu R, Cai D, Li X, Liu B, Chen J, Jiang X, et al. Effects of bisphenol A on reproductive toxicity and gut microbiota dysbiosis in male rats. Ecotoxicol Environ Saf 2022;239:113623. doi:10.1016/j.ecoenv.2022.113623
43. Feng D, Zhang H, Jiang X, Zou J, Li Q, Mai H, et al. Bisphenol A exposure induces gut microbiota dysbiosis and consequent activation of gut-liver axis leading to hepatic steatosis in CD-1 mice. Environ Pollut 2020;265(Pt A):114880. doi:10.1016/j.envpol.2020.114880
44. Polyzos SA, Kountouras J, Deretzi G, Zavos C, Mantzoros CS. The emerging role of endocrine disruptors in pathogenesis of insulin resistance: a concept implicating nonalcoholic fatty liver disease. Curr Mol Med 2012;12(1):68-82. doi:10.2174/156652412798376161
45. Martinez Steele E, Marrón Ponce JA, Cediel G, Louzada MLC, Khandpur N, Machado P, et al. Potential reductions in ultra-processed food consumption substantially improve population cardiometabolic-related dietary nutrient profiles in eight countries. Nutr Metab Cardiovasc Dis 2022;32(12):2739-50. doi:10.1016/j.numecd.2022.08.018
46. Martini D, Godos J, Bonaccio M, Vitaglione P, Grosso G. Ultra-processed foods and nutritional dietary profile: a meta-analysis of nationally representative samples. Nutrients 2021;13(10):3390. doi:10.3390/nu13103390
47. Delpino FM, Figueiredo LM, Bielemann RM, da Silva BGC, Dos Santos FS, Mintem GC, et al. Ultra-processed food and risk of type 2 diabetes: a systematic review and meta-analysis of longitudinal studies. Int J Epidemiol 2022;51(4):1120-41. doi:10.1093/ije/dyab247

48. Rauber F, da Costa Louzada ML, Steele EM, Millett C, Monteiro CA, Levy RB. Ultra-processed food consumption and chronic non-communicable diseases-related dietary nutrient profile in the UK (2008–2014). Nutrients 2018;10(5):587. doi:10.3390/nu10050587
49. Litwinowicz K, Waszczuk E, Gamian A. Advanced glycation end-products in common non-infectious liver diseases: systematic review and meta-analysis. Nutrients 2021;13(10):3370. doi:10.3390/nu13103370
50. Quetglas-Llabrés MM, Monserrat-Mesquida M, Bouzas C, Mateos D, Ugarriza L, Gómez C, et al. Oxidative stress and inflammatory biomarkers are related to high intake of ultra-processed food in old adults with metabolic syndrome. Antioxidants (Basel) 2023;12(8):1532. doi:10.3390/antiox12081532
51. Juul F, Vaidean G, Parekh N. Ultra-processed foods and cardiovascular diseases: potential mechanisms of action. Adv Nutr 2021;12(5):1673-80. doi:10.1093/advances/nmab049

2026 The Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.