scientific reports

Check for updates

OPEN

Diet-induced inflammation is associated with fatty pancreas in patients with common bile duct stones

Maedeh Chegini[1], Mohsen Shaygan Tabar[1], Vahideh Behrouz[2], Mohammad Bahrizadeh[1], Amir Sadeghi[3], Azita Hekmatdoost[1]✉ & Zahra Yari[4]✉

Inflammation has been proven to be associated with chronic diseases. We hypothesized that higher diet-induced inflammation is associated with increased risk of fatty pancreas (FP). Among 278 patients with common bile duct (CBD) stones, 89 patients were diagnosed with fatty pancreas (case group) during endoscopic ultrasonography and the other 189 patients were healthy in this regard (control group). Dietary inflammatory index (DII), empirical dietary inflammatory pattern (EDIP) and dietary inflammatory score (DIS) were calculated based on a 168-question valid food frequency questionnaire. Dietary inflammatory scores were significantly higher in the case group than in the control group. Based on logistic regression analysis, higher scores of DII, EDIP and DIS were significantly associated with higher risk of FP in the crude and adjusted models. In the full adjusted models, higher scores of DII ($OR_{T2\ vs\ T1}$ = 1.36; 95% CI 0.71–2.58 and $OR_{T3\ vs\ T1}$ = 3.3; 95% CI: 1.59–6.8; *P* for trend = 0.001), EDIP ($OR_{T2\ vs\ T1}$ = 1.7; 95% CI 0.89–3.3 and $OR_{T3\ vs\ T1}$ = 2.5; 95% CI 1.2–5.1; *P* for trend = 0.009) and DIS ($OR_{T2\ vs\ T1}$ = 1.48; 95% CI 0.74–2.97 and $OR_{T3\ vs\ T1}$ = 2; 95% CI 1.16–3.63; *P* for trend = 0.040) resulted in increased risk of FP development. Diet-induced inflammation was associated with an increased propensity for developing fatty pancreas.

Keywords Fatty pancreas, Dietary inflammatory index, Common bile duct stones

Abbreviations

BMI	Body mass index
CBD	Common bile duct
CI	Confidence intervals
CRP	C-reactive protein
DII	Dietary inflammatory index
DIS	Dietary inflammatory score
EDIP	Empirical dietary inflammatory pattern
EUS	Endoscopic sonography
FFA	Free fatty acid
FFQ	Food frequency questionnaire
FP	Fatty pancreas
IL	Interleukin
IR	Insulin resistance
IRS	Insulin receptor substrate
Mets	Metabolic syndrome
NAFLD	Non-alcoholic fatty liver disease

[1]Department of Clinical Nutrition and Dietetics, Faculty of Nutrition Sciences and Food Technology, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [2]Department of Nutrition, Faculty of Public Health, Kerman University of Medical Sciences, Kerman, Iran. [3]Research Institute for Gastroenterology and Liver Diseases of Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [4]Department of Nutrition Research, National Nutrition and Food Technology Research Institute and Faculty of Nutrition Sciences and Food Technology, Shahid Beheshti University of Medical Sciences, West Arghavan St. Farahzadi Blvd., Sharake Qods, Tehran, Iran. ✉email: Azita.Hekmatdoost@cw.bc.ca; a_hekmat2000@yahoo.com; zahrayari_nut@yahoo.com

NAFPD	Nonalcoholic fatty pancreas disease
OR	Odds ratios
PUFA	Polyunsaturated fatty acids
SFAs	Saturated fatty acids
T2DM	Type 2 diabetes mellitus
TLR	Toll-like receptors
TNF-α	Tumor Necrosis Factor alpha
WC	Waist circumference

Fat accumulation in the pancreas is characterized by various definitions and terms, such as "pancreatic steatosis (PS)", "fatty pancreas disease" (FPD), "pancreatic lipomatosis", "intra-pancreatic fat deposition (IPFD)" or "nonalcoholic fatty pancreas disease" (NAFPD)[1,2]. However, it is recommended that the term "fatty pancreas" more appropriately describes the accumulation of fat in the pancreas[2]. This pathology outlines the disease's progression from pancreatic fat accumulation to pancreatic inflammation and the development of pancreatic fibrosis and carcinoma[3]. Although the pathophysiology of FP has not been well elucidated, two key mechanisms leading to fat accumulation in the pancreas have been identified[4]. The first is the death of acinar cells and their replacement by adipocytes, and the second is fat accumulation mainly due to obesity, which leads to non-alcoholic fatty pancreatic disease[3,4].

Several factors provoke FP such as congenital diseases, alcohol abuse, infections, hemochromatosis, medications, malnutrition, chronic liver diseases (including non-alcoholic fatty liver disease, chronic hepatitis B, and cirrhosis), metabolic syndrome, and obesity[3,4]. Although the FP precise prevalence is not yet established, multiple studies have reported a range of 16–35%[1]. The main methods in the diagnosis of FP include ultrasound, endoscopic ultrasound, computed tomography, magnetic resonance imaging, and magnetic resonance spectroscopy[3]. According to recent research, FP may be an early manifestation of metabolic syndrome, which is linked to at least twofold increased risk of type 2 diabetes mellitus (T2DM) and hypertension[3,5]. Moreover, FP is significantly related to the occurrence and progression of pancreatic carcinoma, which causes over 331,000 deaths annually and ranks as the 7th global leading cause of cancer-related mortality[4].

Based on research, the risk of ectopic fat deposition in the organs is enhanced by sedentary lifestyles with poor physical activity, obesogenic diets, metabolic syndrome, and differential visceral fat storage[4,6]. Although there is no standard treatment for FP as such, increased levels of adipose tissue in the pancreas seem to be reversible, implying that FP can be altered by dietary modifications, increased physical activity, and adopting healthy lifestyle[7,8]. FP may also exacerbate local inflammation, as adipocytes are involved in the release of pro-inflammatory cytokines and chemokines through Toll-like receptor (TLR)-mediated signaling[1,9]. To date, several studies have linked dietary components to either inhibiting or promoting inflammatory processes[10]. Excessive consumption of high-fat dairy products, red meats, and refined grains has been related to elevated inflammation, whereas diets rich in fruits and green vegetables, fish, and whole grains have been linked to improved inflammatory markers[10,11]. On the other hand, various nutrients such as complex carbohydrates, n-3 polyunsaturated fatty acids (PUFA), vitamin E, Fiber, vitamin C, b-carotene, and magnesium have frequently been associated with decreased levels of inflammation[10,12].

According to the studies, fatty infiltration of the pancreas is associated with chronic inflammation[1]. However, the association of diet-induced inflammation and FP is still unclear[3]. In this research, we hypothesized that higher dietary inflammatory indices is associated with increased risk of fatty pancreas in patients with common bile duct (CBD) stones. To the best of our knowledge, this is the first study that investigated the relationship between FP and dietary inflammatory indices.

Methods and materials

Study design and population

278 adults with common bile duct (CBD) stones in endoscopic sonography (EUS) results were enrolled in this case–control study from 1 July 2022 to 30 May 2023. The sample size was calculated using a significance level of 5%, $Z_{1-\alpha/2}=1.96$, 80% power, $Z_{1-\beta}=0.84$, odds ratio = 3. A minimum sample size of 80 subjects was calculated. Double this number was considered for the control group. The study was approved by the Research Ethics Committee of Shahid Beheshti Medical University of Iran, under protocol number IR.SBMU.RETECH.REC.1402.689. All participants underwent EUS by a gastro-hepatology specialist. Eligible patients were chosen by consecutive-sampling method and provided written informed consent, prior to the study enrollment. FP was diagnosed via EUS findings in accordance with relevant guidelines[13]. Compared to computed tomography and magnetic resonance imaging, endoscopic ultrasound examination provides superior visualization and evaluation of the examined gland[3]. Demographic data and clinical characteristics were obtained via face-to-face interviews, which were then cross-checked with patients' medical records, if available.

Inclusion and exclusion criteria

This study recruited conscious patients over the age of 18 who referred to the gastroenterology clinic of Ayatollah Taleghani Hospital, Tehran, Iran. Patients in the FP group (n = 89) were clinically diagnosed with fatty pancreas plus CBD stones in EUS findings, whereas the control group (n = 189) included those who had solely a diagnosis of CBD stones. Since in most cases, FP is an incidental finding during transabdominal ultrasound[14], in this study, patients suspected of having CBD stones underwent EUS for diagnosis, during which fatty pancreas was detected as an incidental finding. Although pancreatic biopsy is the best method for measuring pancreatic fat, EUS is still considered the most sensitive investigation for pancreatic screening[15]. In FP, the pancreas becomes hypodense and shows typical hyperechogenicity on ultrasound examination[14]. Individuals with ongoing

pregnancy or breastfeeding, active malignancy, and severe comorbid diseases such as hepatitis, pancreatitis, cirrhosis, and renal failure (Cr Cl < 30 mL/min) were not included in both groups Fig. 1.

Anthropometric measurements

Each patient's weight was measured in kilograms over light clothing in a standing position, to the nearest 100 g using a calibrated scale (Seca, Germany). The height of each participant was measured without shoes by a meter mounted on the wall to the nearest 0.5 cm[16]. The waist circumference (WC) was also assessed using an unstretched shape tape measure by standard methods at the umbilical level, with light clothing, and without any pressure to the body surface to the nearest 0.1 cm[16]. Afterward, the body mass index (BMI) was computed by dividing the weight (kg) by the square of height (m^2).

Dietary assessments

A validated 168-item semi-quantitative food frequency questionnaire (FFQ) was used for dietary intake examination[17]. The FFQ was completed by an expert dietitian being unaware of the patients' condition (regarding having FP or not) via face-to-face interviews. This questionnaire provided daily, weekly, monthly and yearly frequency of food intake over the previous year. This information was subsequently converted to grams per day using household measures[18]. Total energy and dietary nutrient intakes were then analyzed using Nutritionist 4 software (First Databank Inc., Hearst Corp., San Bruno, CA, USA) modified for Iranian foods.

Calculation of dietary inflammatory indices

The dietary inflammatory index (DII) was first developed by Shivappa et al., which is based on 45 dietary factors[19,20]. The DII validity has been assessed in previous research and is known to predict concentrations of 6 inflammatory biomarkers including interleukin (IL)-1β, IL-6, Tumor Necrosis Factor alpha (TNF-α), C-reactive protein (CRP), IL-4, and IL-10[19]. Although the DII is primarily nutrient-based, it also includes frequently consumed components of the diet such as flavonoids, spices, and tea[10]. On the other hand, the empirical dietary inflammatory pattern (EDIP) is entirely based on 15 food groups including processed meat, red meat, organ meat, other fish, other vegetables, refined grains, high-energy beverages, tomatoes, tea, coffee, dark yellow vegetables, leafy green vegetables, snacks, fruit juice, and pizza[19]. The EDIP was recently established and has been validated in several cross-sectional and cohort studies[21,22]. Whereas the EDIP and DII both evaluate the inflammatory potential of the diet, there is only a modest correlation between the two dietary indices, implying that they contain separate information not captured by the other[19]. While the DII and EDIP have been generated to identify dietary contributions to systemic inflammation, the dietary inflammation score (DIS) quantifies the contributions of lifestyle to inflammation[23]. The DIS has 19 components and its validity was previously examined in studies[23]. In the current research, we examined all three inflammatory indicators according to previous reports[20,21,23].

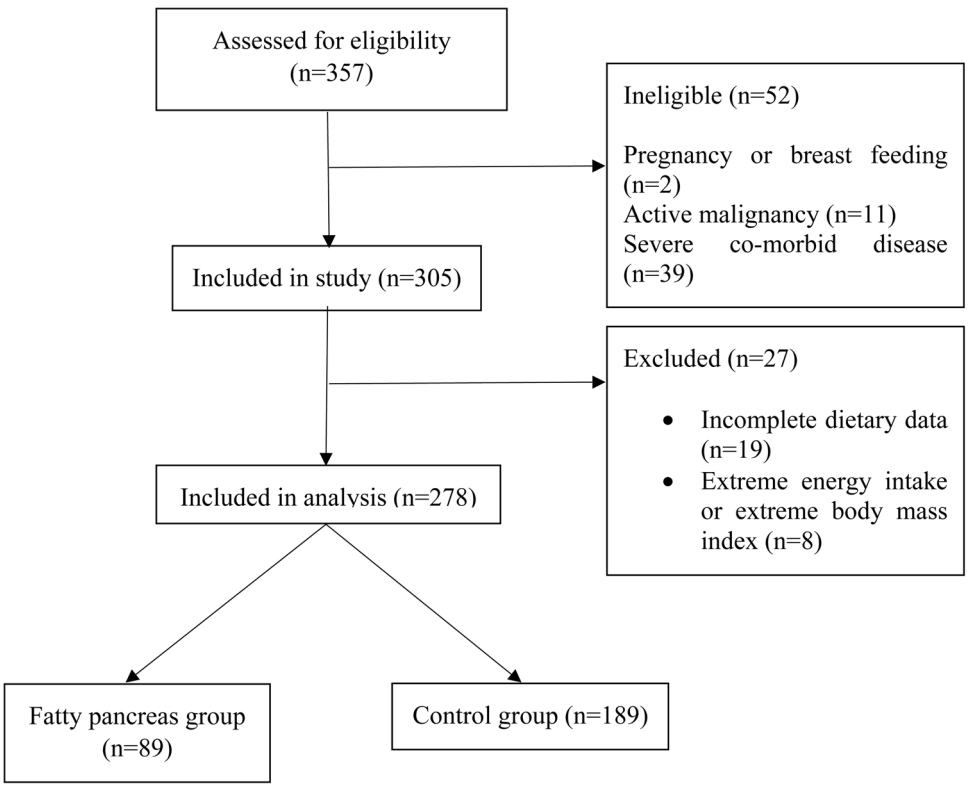

Fig. 1. Flow chart of study enrollment.

Initially, to construct the DII[20], we used the reported global means and standard deviations to compute a z score for each component [based on total micronutrient intakes]. We subsequently produced normalized, centered percentiles for each component, and multiplied them by their reported respective weight. Ultimately, each participant's total DII score was determined by adding up the individual DII scores of each component. To develop the EDIP score, the servings of intake for each of the 15 EDIP food groups were formed as described by Tabung et al.[21], and were then multiplied by their reported weights. Lastly, the residual method was utilized to adjust the final values for energy intake[24]. We assessed the overall DIS score by considering 18 food groups that include leafy greens and cruciferous vegetables, tomatoes, apples and berries, deep yellow or orange vegetables and fruit, other fruits and real fruit juices, other vegetables, legumes, fish, poultry, red and organ meats, processed meats, added sugars, high-fat dairy, low-fat dairy, coffee and tea, nuts, other fats, and refined grains and starchy vegetables[23]. Following the standardization of each food group, the values were totaled. The "My Pyramid Equivalents Database"[25] was used to disaggregate mixed dishes (e.g., pizza, spaghetti) in the FFQ. The disaggregated components were then added to their respective DIS food groups. A higher score on all three indices implies an enhanced balance of pro- to anti-inflammatory dietary intakes.

Data analyses

The statistical package for social sciences version 21.0 for Windows (SPSS Inc., Chicago, IL) was used to perform analysis, and *P*-values < 0.05 were considered statistically significant. Following data cleaning, the normality of data was examined using a histogram chart and Kolmogorov–Smirnov test. Initially, participants were categorized into 3 groups based on 33rd and 66th percentile values for the DII, EDIP, and DIS scores. The qualitative variables between DII tertiles were compared using Chi-square or Fisher's exact test and the results were expressed as count (percentage). For quantitative variables one way ANOVA was applied and the results were reported as mean ± SD. Comparisons of dietary intakes across tertiles of DII, EDIP, and DIS were carried out by the use of one-way ANOVA. Furthermore, the association of DII, EDIP, and DIS with FP was evaluated using binary logistic regression. Three models were synthesized to annihilate the effect of potential confounders for DII, EDIP, and DIS tertials, which have been provided with odds ratios (ORs) and 95% confidence intervals (CIs). The first model was defined as crude. In the second model, age and gender and in the third model, in addition to them, BMI and energy intake were considered as confounders. In all analyses, the first tertiles were considered as the reference category.

Results

A comparison of the basic characteristics of the participants in the case group (patients with fatty pancreas and common bile duct stones) and the control group (patients with common bile duct stones) is shown in Table 1. Significant differences were observed between the two groups in anthropometric measurements, except waist circumference, and macronutrient percentages, as well as dietary inflammatory scores. The basic characteristics of the participants were compared according to the tertiles of DII in Table 2. No difference was found in the demographic information of the participants. Although there was a significant difference in weight and height between tertiles, this significance was not found in the comparison of BMI. The comparison of dietary intakes showed that with the increase in DII score, energy intake and the percentage of carbohydrates increased significantly, but no difference was observed in the percentage of protein and fat. Also, with the increase in the

	Case	Controls	*P* value
Age, y	56.9 ± 15.1	55.2 ± 15.2	0.388
Male, %	41	59	0.010
Weight, kg	81.6 ± 17.1	71.5 ± 14.5	< 0.001
Height, cm	167.6 ± 10.1	162.7 ± 8.3	< 0.001
BMI, kg/m^2	29 ± 5.3	26.9 ± 5.1	0.003
Waist circumference, cm	105.3 ± 13.2	101.4 ± 14.1	0.965
Smoking, %	12	16.4	0.337
Alcohol, %	3.7	3.2	0.838
Energy (Kcal/d)	2631 ± 879	2554 ± 1104	0.575
Carbohydrate (%)	58 ± 22	52 ± 9	< 0.001
Protein (%)	14 ± 3	13 ± 4	< 0.001
Fat (%)	30 ± 6	33 ± 5	< 0.001
DII	0.99 ± 1.1	0.59 ± 0.43	< 0.001
EDIP	0.7 ± 0.51	0.5 ± 0.44	0.001
DIS	− 7.2 ± 399	− 103.6 ± 242	0.014

Table 1. Comparison of basic characteristics of cases (patients with fatty pancreas and common bile duct stone) and controls (patients with common bile duct stone). Data are presented as mean (SD) for continuous variable and percent for categorical variables. Independent t-test for quantitative variables and χ^2 test for qualitative variables. *BMI* body mass index, *DII* dietary inflammatory index, *EDIP* empirical dietary inflammatory pattern, *DIS* dietary inflammatory score.

	Dietary inflammatory index			
	T1	T2	T3	*P* value
Cases, n (%)	16 (17)	33 (38)	40 (45)	< 0.001
Age, y	55.8 ± 14.5	57.2 ± 15.2	53.9 ± 15.9	0.367
Male, %	26	37	40	0.124
Weight, kg	71.5 ± 14.2	73.9 ± 15.3	78.4 ± 18.1	0.013
Height, cm	162.1 ± 8.3	164.7 ± 9.1	165.9 ± 9.6	0.015
BMI, kg/m^2	27.2 ± 5.1	27.2 ± 5.2	28.4 ± 5.4	0.212
Waist circumference, cm	106 ± 11.9	105.4 ± 16.5	104.9 ± 11.2	0.965
Smoking, %	26.8	31.7	41.5	0.381
Alcohol, %	22.2	22.2	55.6	0.326
Dietary intakes				
Energy (Kcal/d)	2375 ± 954	2501 ± 777	2846 ± 1279	0.007
Carbohydrate (%)	51 ± 9	53 ± 15	57 ± 20	0.031
Protein (%)	12 ± 3	13 ± 4	14 ± 4	0.141
Fat (%)	39 ± 9	38 ± 10	37 ± 10	0.146
DII	0.25 ± 0.11	0.59 ± 0.1	1.3 ± 0.9	< 0.001
EDIP	0.24 ± 0.11	0.59 ± 0.11	1.4 ± 0.64	< 0.001
DIS	− 12 ± 390	− 95 ± 199	− 112.4 ± 283	0.056

Table 2. Basic characteristics of study participants based on tertiles of dietary inflammatory index. Data are presented as mean (SD) for continuous variable and number (percent) for categorical variables. ANOVA for quantitative variables and χ^2 test for qualitative variables. *BMI* body mass index, *DII* dietary inflammatory index, *EDIP* empirical dietary inflammatory pattern, *DIS* dietary inflammatory score.

DII score, the EDIP score also increased significantly ($P < 0.001$), but the changes in the DIS score were close to the significant level ($P = 0.05$).

The comparison of dietary components of EDIP and DIS are displayed in Table 3. As the inflammatory score increased, intake of processed meats, red meat, refined grains, energy drinks and some vegetables such as tomatoes increased significantly. The analysis of DIS components also indicated a significant increase in intakes of processed meats, high-fat dairy products, refined grains, and starchy vegetables, as well as a significant decrease in intakes of some vegetables, fruits, coffee, and tea.

Table 4 describes the risk of developing FP based on scores of different indices of dietary inflammation. The number of cases increased significantly with the increase in the scores of all three inflammatory indices. Based on logistic regression analysis, higher scores of DII, EDIP and DIS were significantly associated with higher risk of FP in all three models of analysis. Although in pairwise comparisons, it was found that this relationship was significant only between the third and first tertiles, but the confidence interval indicated that this increase in risk of FP in the second tertile is not significant compared to the reference.

In the crude models, higher scores of DII ($OR_{T2\ vs\ T1} = 1.38$; 95% CI 0.76–2.5 and $OR_{T3\ vs\ T1} = 3.85$; 95% CI 1.9–7.7; *P* for trend < 0.001), EDIP ($OR_{T2\ vs\ T1} = 1.99$; 95% CI 1.1–3.7 and $OR_{T3\ vs\ T1} = 2.78$; 95% CI 1.46–5.3; *P* for trend = 0.002) and DIS ($OR_{T2\ vs\ T1} = 1.1$; 95% CI 0.61–2 and $OR_{T3\ vs\ T1} = 1.98$; 95% CI 1–3.8; *P* for trend = 0.016) resulted in increased risk of FP development. Additionally, adjustment for age and sex and further for energy intake and BMI yielded similar results. The direct and significant relationship between dietary inflammatory indices and the risk of fatty pancreas, after adjustment for all confounders, is shown in Fig. 2.

Discussion

The current case–control study yielded some fascinating findings regarding the association between diet-induced inflammation and the risk of fatty pancreas. The findings of the present study, for the first time, showed that higher scores of DII, EDIP and DIS were significantly associated with higher risk of fatty pancreas, which confirms the hypothesis of the study.

Many studies have addressed the fundamental role of inflammation in the pathophysiology of chronic diseases, but the role of diet-induced inflammation in FP has not been addressed yet. A recently published paper on the Nurses' Health Study II cohort described that a higher EDIP score was associated with an increased risk of non-alcoholic fatty liver disease (NAFLD) and cirrhosis[26]. FP is closely related to NAFLD, in most cases of FP, traces of fatty liver can also be found and the amount of fat accumulated in the pancreas is directly linked to the degree of liver steatosis observed during histological examination[27,28]. NAFLD is a chronic disease characterized by low-grade inflammation and the development and progression of the disease is accelerated by increased levels of pro-inflammatory cytokines such as IL-1, TNF-α, and IL-6, along with the overproduction of adipokines[29]. These inflammatory mediators trigger a cascade of processes such as liver inflammation and apoptosis, lipotoxicity, and fibrosis[29]. Inadequate consumption of anti-inflammatory foods, as indicated by high DII, DIS, and EDIP scores, may lead to fat buildup in liver and possibly pancreatic cells, leading to cell dysfunction by causing lipotoxicity. This process is initiated by the activation of the inflammatory pathway and ultimately accelerates the progression of the disease[30].

	Tertiles			
	T1	T2	T3	*P* value
EDIP component (serving/day)				
Processed meat	0.005 (0.002, 0.008)	0.02 (0.006, 0.04)	0.05 (0.02, 0.07)	0.005
Red meat	0.17 (0.13, 0.2)	0.19 (0.15, 0.24)	0.3 (0.2, 0.4)	0.005
Organ meat	0.02 (0, 0.04)	0.02 (0.01, 0.03)	0.02 (0.01, 0.03)	0.936
Other fish	0.07 (0.05, 0.1)	0.09 (0.07, 0.13)	0.1 (0.08, 0.15)	0.179
Other vegetables	0.87 (0.75, 1)	1.5 (1.3, 1.7)	2.9 (2.5, 3.4)	< 0.001
Refined grains	1.7 (1.5, 2)	3.3 (2.9, 3.6)	7.5 (6.3, 8.6)	< 0.001
High-energy beverages	0.1 (0.05, 0.16)	0.18 (0.11, 0.24)	0.4 (0.2, 0.5)	< 0.001
Tomatoes	0.5 (0.4, 0.6)	0.8 (0.7, 0.9)	1 (0.8, 1.2)	< 0.001
Tea	3.2 (2.8, 3.6)	2.7 (2.3)	2.8 (2.3)	0.229
Coffee	0.05 (0.01, 0.09)	0.02 (0.005, 0.04)	0.08 (0.03, 0.1)	0.080
Dark yellow vegetables	0.18 (0.1, 0.25)	0.18 (0.14, 0.22)	0.18 (0.14, 0.22)	0.998
Leafy green vegetables	0.44 (0.34, 0.54)	0.35 (0.27, 0.73)	0.42 (0.32, 0.52)	0.342
Snacks	0.08 (0.04, 0.13)	0.12 (0.05, 0.19)	0.23 (0.08, 0.38)	0.091
Fruit juice	0.07 (0.02, 0.13)	0.06 (0.03, 0.09)	0.09 (0.02, 0.15)	0.697
Pizza	0.005 (0.002, 0.009)	0.01 (0.004, 0.018)	0.03 (0.007, 0.02)	0.054
DIS component (g/d)				
Leafy greens and cruciferous vegetables	27.5 (21.9, 33.1)	19.4 (15, 23.9)	19.2 (14.1, 24.3)	0.033
Tomatoes	138.9 (116.8, 161.1)	86.2 (73.5, 98.9)	66.7 (54, 79.4)	< 0.001
Apples and berries	111.9 (84.7, 139.3)	66.5 (53.5, 79.6)	59.9 (45.9, 73.9)	< 0.001
Deep yellow or orange vegetables and fruit	60.5 (44.9, 76.1)	37.1 (27.9, 46.3)	33.3 (24.3, 42.4)	0.002
Other fruits and real fruit juices	389.7 (306.9, 427.5)	244.6 (208.3, 280.9)	198.5 (164.9, 232.1)	< 0.001
Other vegetables	199.1 (169.2, 229.1)	148.4 (127.9, 168.9)	142.7 (109.1, 176.2)	0.010
Legumes	36.9 (28.8, 45)	29.5 (23.9, 35.1)	30.5 (25.3, 35.7)	0.219
Fish	11.9 (8.2, 15.6)	9.2 (6.1, 12.3)	11.2 (7.6, 14.8)	0.536
Poultry	36.9 (30.7, 43.1)	32 (26.6, 37.4)	34.9 (29.5, 40.3)	0.480
Red and organ meats	53.1 (39.7, 66.4)	43.6 (35.1, 52.2)	51.8 (43.5, 60.1)	0.385
Processed meats	1.3 (0.8, 1.8)	2.6 (0.8, 4.4)	6.6 (2.5, 10.8)	0.014
Added sugars	118.1 (90, 146.2)	101.9 (67.7, 136)	119.2 (87.2, 151.2)	0.688
High-fat dairy	218.4 (149.3, 287.5)	142.1 (103.7, 180.5)	133.6 (94.1, 173)	0.038
Low-fat dairy	111.1 (86.8, 135.5)	113.3 (81.7, 144.8)	120.1 (85.6, 154.5)	0.911
Coffee and tea	990.1 (862.1, 1117.9)	656.2 (577.6, 734.9)	479.9 (417.8, 541.9)	< 0.001
Nuts	22 (10.9, 33.1)	10.9 (7.7, 14)	13.7 (9.3, 18.1)	0.077
Other fats	58.4 (50.8, 66)	52 (44.9, 59.4)	55.7 (48.3, 63.1)	0.490
Refined grains and starchy vegetables	348.8 (299.2, 398.3)	413.8 (378.3, 448.9)	724.6 (631.4, 817.8)	< 0.001

Table 3. The intakes of empirical dietary inflammatory pattern (EDIP) and dietary inflammatory score (DIS) components in the study population according to the tertiles of dietary inflammatory index. Data are presented as mean (95% CI) based on ANOVA test.

The protective role of anti-inflammatory compounds, including fruits, vegetables, fiber, and coffee, against FP, as well as the direct association of inflammatory dietary components, such as saturated fats, red meat, and cholesterol, with acute and chronic pancreatitis, has also been demonstrated[31–33]. Similarly, studies have pointed out the relationship between dietary inflammatory indicators and the risk of T2DM, insulin resistance (IR) and metabolic syndrome (Mets)[34,35], which are related to FP. Although the results in this regard have been contradictory and some studies failed to demonstrate a significant relationship[36,37]. On the one hand, it has been shown that diet-induced chronic inflammation can contribute to an increased risk of diabetes. In fact, this persistent inflammation can cause IR and disrupt the function of pancreatic beta cells, ultimately contributing to DM[38]. On the other hand, it has been stated that IR[14] and metabolic syndrome and its components such as DM are directly related to the incidence of FP[5,39].

The excessive production of inflammatory factors leads to the activation of c-Jun N-terminal kinase, causing the phosphorylation of insulin receptor substrate-1 (IRS-1) at Ser307. This phosphorylation results in the deactivation of IRS-1, ultimately blocking insulin receptor signaling[40,41]. Inflammatory mediators hinder insulin-dependent glucose transport by inducing the suppressor of cytokine signaling-3[42]. Inflammatory factors also inhibit lipoprotein lipase activity, which decreases peripheral glucose utilization[42]. Elevation of inflammatory markers in low-grade inflammation contributes to the development of diabetes and IR and their consequent diseases[43–45]. In addition, excessive consumption of pro-inflammatory foods such as saturated fat and animal protein can potentially accelerate the development of diabetes and IR and related diseases[46,47]. Diets high in

	Tertiles of scores			
	T1	T2	T3	*P* trend
DII				
Median score	0.26 (0.17, 0.32)	0.59 (0.58, 0.67)	1.11 (0.92, 1.37)	
Case (n)	15	32	39	
Model 1	1 (ref)	1.38 (0.76, 2.5)	3.85 (1.9, 7.7)	< 0.001
Model 2	1 (ref)	1.54 (0.83, 2.86)	3.65 (1.82, 7.37)	< 0.001
Model 3	1 (ref)	1.36 (0.71, 2.58)	3.3 (1.59, 6.8)	0.001
EDIP				
Median score	0.15 (0.08, 0.23)	0.47 (0.38, 0.53)	0.9 (0.75, 1.28)	
Case (n)	21	27	41	
Model 1	1 (ref)	1.99 (1.1, 3.7)	2.78 (1.46, 5.3)	0.002
Model 2	1 (ref)	1.87 (0.99, 3.54)	2.42 (1.2, 4.7)	0.008
Model 3	1 (ref)	1.7 (0.89, 3.3)	2.5 (1.2, 5.1)	0.009
DIS				
Median score	− 312.9 (− 419.6, − 236.7)	− 80.3 (− 123.1, − 40.87)	141.8 (56.7, 228)	
Case (n)	22	32	35	
Model 1	1 (ref)	1.1 (0.61, 2)	1.98 (1, 3.8)	0.016
Model 2	1 (ref)	1.03 (0.55, 1.9)	1.7 (0.87, 3.3)	0.022
Model 3	1 (ref)	1.48 (0.74, 2.97)	2 (1.16, 3.63)	0.040

Table 4. Odds ratio (95% CI) fatty pancreas risk according to tertiles of dietary inflammatory indices scores. Multiple logistic regression models for estimating ORs and 95% CIs. Model 1: Crude. Model 2: Adjustment for age, sex. Model 3: Adjustment for age, sex, BMI, energy intake. *DII* dietary inflammatory index, *EDIP* empirical dietary inflammatory pattern, *DIS* dietary inflammatory score.

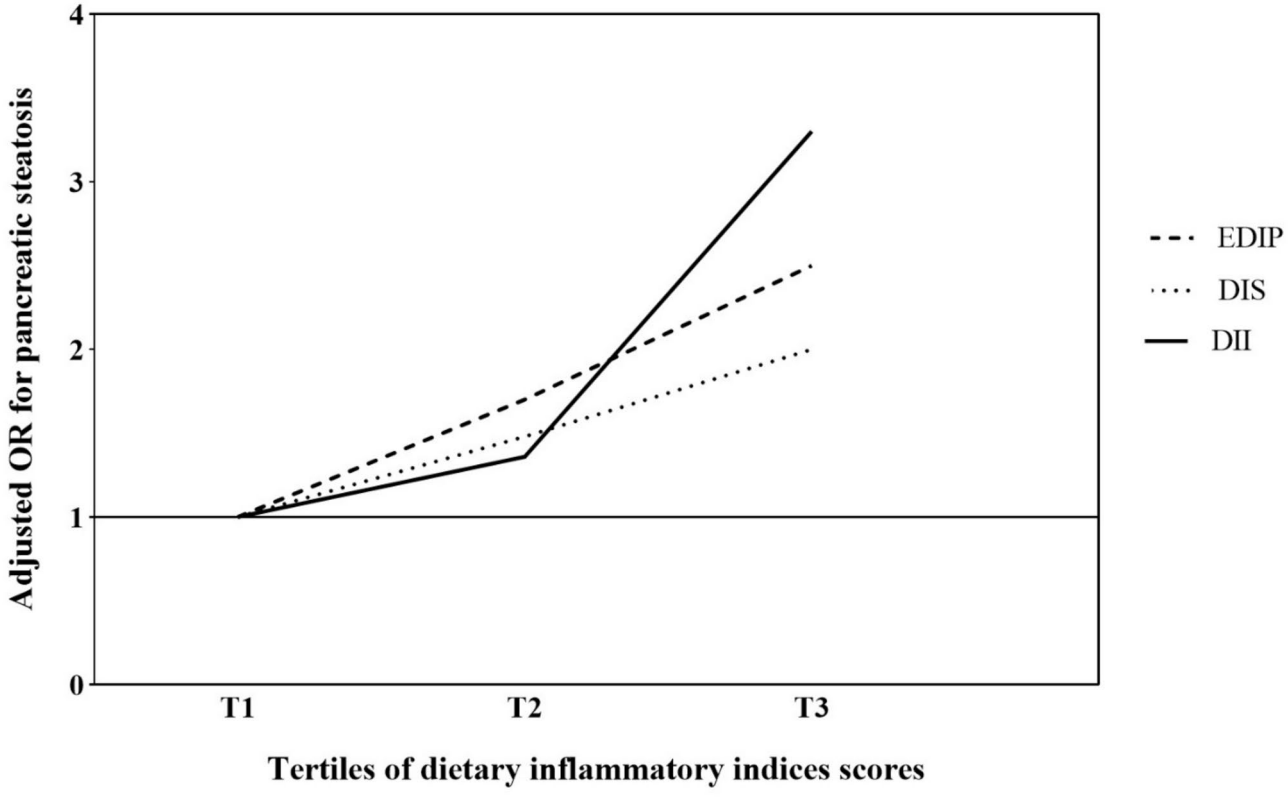

Fig. 2. The association between dietary inflammatory indices and the risk of fatty pancreas. *DII* dietary inflammatory index, *EDIP* empirical dietary inflammatory pattern, *DIS* dietary inflammatory score.

saturated fatty acids (SFAs) can elevate endotoxin levels and induce low-grade inflammation as a consequence of enhanced intestinal absorption of endotoxins resulting from lipid digestion[48]. It has been shown that pro-inflammatory diet has a significant relationship with increased triglyceride[49]. Triglyceride increases inflammation by increasing free fatty acid (FFA) oxidation, which in turn can cause pancreatic cell dysfunction[50,51].

An important strength of this study is that the present study is the first to investigate the association between dietary inflammatory indices and FP. Another important strength is the use of a valid and reproducible FFQ. This allowed for a comprehensive assessment of the main sources of nutrients in the diet, although some measurement errors may have occurred in FFQ. Controls were carefully selected by ensuring none of them had diet-related diseases or other major risk factors of FP.

In addition to the positive aspects of this study, it is important to acknowledge certain limitations that need to be considered. As with other case–control studies, the possibility of recall bias and selection bias in this study is inevitable, but the use of reliable FFQs administered by trained interviewers might have decreased the risk of recall bias. Other limitations of using an FFQ to assess dietary intake include potential inaccuracies in reporting and limited food choices. Moreover, the participants in this study were patients with CBD stones, so the generalization of the results requires further studies.

Conclusion

In conclusion, our case–control study suggested that higher scores of EDIP, DII, and DIS are related to increased odds of FP in patients with CBD stones.

Data availability

The datasets analyzed in the current study are available from the corresponding author on reasonable request.

Received: 24 December 2024; Accepted: 24 April 2025
Published online: 05 May 2025

References

1. Caldart, F., de Pretis, N., Luchini, C., Ciccocioppo, R. & Frulloni, L. Pancreatic steatosis and metabolic pancreatic disease: A new entity?. *Int. Emerg. Med.* **18**(8), 2199–2208 (2023).
2. Petrov, M. S. & Taylor, R. Intra-pancreatic fat deposition: Bringing hidden fat to the fore. *Nat. Rev. Gastroenterol. Hepatol.* **19**(3), 153–168 (2022).
3. Sattarovich, B. A. & Shamsitdinovna, P. S. Pancreatic steatosis is a new therapeutic problem in gastroenterology (Literature Review). *Galaxy Int. Interdiscip. Res. J.* **10**(9), 209–218 (2022).
4. Truong, E., Pandol, S. & Jeon, C. Uniting epidemiology and experimental models: pancreatic steatosis and pancreatic cancer. *EBioMedicine* **79**, 103996 (2022).
5. Bi, Y., Wang, J. L., Li, M. L., Zhou, J. & Sun, X. L. The association between pancreas steatosis and metabolic syndrome: A systematic review and meta-analysis. *Diab. Metab. Res. Rev.* **35**(5), e3142 (2019).
6. Hens, W. et al. The effect of lifestyle interventions on excess ectopic fat deposition measured by noninvasive techniques in overweight and obese adults: A systematic review and meta-analysis. *J. Phys. Act. Health* **13**(6), 671–694 (2016).
7. Pang, C. et al. Non-alcoholic Fatty pancreas disease (NAFPD): An updated review. *J. Pancreatol.* **7**(03), 212–221 (2024).
8. DellaPepa, G., Salamone, D., Testa, R., Bozzetto, L. & Costabile, G. Intrapancreatic fat deposition and nutritional treatment: the role of various dietary approaches. *Nutrit. Rev.* **82**(12), 1820–1834 (2024).
9. Gerst, F. et al. Metabolic crosstalk between fatty pancreas and fatty liver: Effects on local inflammation and insulin secretion. *Diabetologia* **60**, 2240–2251 (2017).
10. Shivappa, N. et al. Associations between dietary inflammatory index and inflammatory markers in the Asklepios Study. *Br. J. Nutr.* **113**(4), 665–671 (2015).
11. Mukherjee, M. S., Han, C. Y., Sukumaran, S., Delaney, C. L. & Miller, M. D. Effect of anti-inflammatory diets on inflammation markers in adult human populations: A systematic review of randomized controlled trials. *Nutr. Rev.* **81**(1), 55–74 (2023).
12. Stumpf, F., Keller, B., Gressies, C. & Schuetz, P. Inflammation and nutrition: Friend or foe?. *Nutrients* **15**(5), 1159 (2023).
13. Van Der Merwe, S. W. et al. Therapeutic endoscopic ultrasound: European society of gastrointestinal endoscopy (ESGE) guideline. *Endoscopy* **54**(02), 185–205 (2022).
14. Paul, J. & Shihaz, A. V. H. Pancreatic steatosis: A new diagnosis and therapeutic challenge in gastroenterology. *Arq. Gastroenterol.* **57**, 216–220 (2020).
15. Lesmana, C. R. A., Ho, K. Y. & Lesmana, L. A. Impact of endoscopic ultrasound procedures in various pancreatobiliary disorders in Indonesia based on a case series in a private hospital. *Case Rep. Gastroenterol.* **9**(2), 206–214 (2015).
16. Mahan, L. K. & Raymond, J. L. *Krause's Food and the Nutrition Care Process-e-Book* (Elsevier Health Sciences, 2016).
17. Esmaillzadeh, A., Mirmiran, P. & Azizi, F. Whole-grain intake and the prevalence of hypertriglyceridemic waist phenotype in Tehranian adults. *Am. J. Clin. Nutr.* **81**(1), 55–63 (2005).
18. Ghaffarpour, M., Houshiar-Rad, A. & Kianfar, H. The manual for household measures, cooking yields factors and edible portion of foods. *Tehran: Nashre Olume Keshavarzy* **7**(213), 42–58 (1999).
19. Tabung, F. K. et al. An empirical dietary inflammatory pattern score enhances prediction of circulating inflammatory biomarkers in adults. *J. Nutr.* **147**(8), 1567–1577 (2017).
20. Shivappa, N., Steck, S. E., Hurley, T. G., Hussey, J. R. & Hébert, J. R. Designing and developing a literature-derived, population-based dietary inflammatory index. *Public Health Nutr.* **17**(8), 1689–1696 (2014).
21. Tabung, F. K. et al. Development and validation of an empirical dietary inflammatory index. *J. Nutr.* **146**(8), 1560–1570 (2016).
22. Norde, M. M., Tabung, F. K., Giovannucci, E. L., Fisberg, R. M. & Rogero, M. M. Validation and adaptation of the empirical dietary inflammatory pattern across nations: A test case. *Nutrition* **79**, 110843 (2020).
23. Byrd, D. A. et al. Development and validation of novel dietary and lifestyle inflammation scores. *J. Nutr.* **149**(12), 2206–2218 (2019).
24. Willett, W. C., Howe, G. R. & Kushi, L. H. Adjustment for total energy intake in epidemiologic studies. *Am. J. Clin. Nutr.* **65**(4), S1220–S1228 (1997).
25. Bowman, S. A., Friday, J. E. & Moshfegh, A. J. *MyPyramid Equivalents Database, 20 for USDA Survey Foods, 2003–2004: Documentation and User Guide* (U.S Department of Agriculture, 2008).
26. Ibrahim, M. K. et al. The empirical dietary inflammatory pattern score and the risk of nonalcoholic fatty liver disease and cirrhosis. *Hepatol. Commun.* **7**(10), e0263 (2023).

27. Wu, W. C. & Wang, C. Y. Association between non-alcoholic fatty pancreatic disease (NAFPD) and the metabolic syndrome: Case-control retrospective study. *Cardiovasc. Diabetol.* **12**, 77 (2013).
28. Nacif, L. S. et al. Liver biopsy may facilitate pancreatic graft evaluation: Positive association between liver steatosis and pancreatic graft adipose infiltration. *Clinics (Sao Paulo)* **73**, e49 (2018).
29. Luo, Y. & Lin, H. Inflammation initiates a vicious cycle between obesity and nonalcoholic fatty liver disease. *Immun. Inflamm. Dis.* **9**(1), 59–73 (2021).
30. Farhadnejad, H. et al. The association between dietary inflammation scores and non-alcoholic fatty liver diseases in Iranian adults. *BMC Gastroenterol.* **22**(1), 267 (2022).
31. Oskarsson, V., Sadr-Azodi, O., Orsini, N., Andrén-Sandberg, Å. & Wolk, A. Vegetables, fruit and risk of non-gallstone-related acute pancreatitis: A population-based prospective cohort study. *Gut* **62**(8), 1187–1192 (2013).
32. Mao, X. et al. Association between dietary habits and pancreatitis among individuals of european ancestry: A two-sample Mendelian randomization study. *Nutrients* **15**(5), 1153 (2023).
33. Setiawan, V. W. et al. Dietary factors reduce risk of acute pancreatitis in a large multiethnic cohort. *Clin. Gastroenterol. Hepatol.* **15**(2), 257–65.e3 (2017).
34. Lee, D. H. et al. Dietary inflammatory and insulinemic potential and risk of type 2 diabetes: Results from three prospective US cohort studies. *Diab. Care* **43**(11), 2675–2683 (2020).
35. Shakeri, Z. et al. Empirical dietary inflammatory pattern and risk of metabolic syndrome and its components: Tehran Lipid and Glucose Study. *Diabetol. Metab. Syndr.* **11**, 1–9 (2019).
36. Sokol, A. et al. Association between the dietary inflammatory index, waist-to-hip ratio and metabolic syndrome. *Nutr. Res.* **36**(11), 1298–1303 (2016).
37. Pimenta, A. M. et al. Dietary indexes, food patterns and incidence of metabolic syndrome in a Mediterranean cohort: The SUN project. *Clin. Nutr.* **34**(3), 508–514 (2015).
38. Li, Z.-Z., Liu, J.-B., Li, L., Jiao, L. & Chen, L. Intensive therapy for diabetes through influence on innate immune system. *Med. Hypotheses* **72**(6), 675–676 (2009).
39. Tirkes, T. et al. Association of pancreatic steatosis with chronic pancreatitis, obesity, and type 2 diabetes mellitus. *Pancreas* **48**(3), 420–426 (2019).
40. Kohn, L. D., Wallace, B., Schwartz, F. & McCall, K. Is type 2 diabetes an autoimmune-inflammatory disorder of the innate immune system?. *Endocrinology* **146**(10), 4189–4191 (2005).
41. Hirosumi, J. et al. A central role for JNK in obesity and insulin resistance. *Nature* **420**(6913), 333–336 (2002).
42. Karlsen, A. E. et al. Suppressor of cytokine signaling 3 (SOCS-3) protects β-cells against interleukin-1β-and interferon-γ-mediated toxicity. *Proc. Natl. Acad. Sci.* **98**(21), 12191–12196 (2001).
43. Weisberg, S. P. et al. Obesity is associated with macrophage accumulation in adipose tissue. *J. Clin. Investig.* **112**(12), 1796–1808 (2003).
44. Kim, C. et al. Circulating levels of MCP-1 and IL-8 are elevated in human obese subjects and associated with obesity-related parameters. *Int. J. Obes.* **30**(9), 1347–1355 (2006).
45. Kato, K. et al. Association between elevated C-reactive protein levels and prediabetes in adults, particularly impaired glucose tolerance. *Can. J. Diab.* **43**(1), 40-45.e2 (2019).
46. Chen, Z. et al. Associations of specific dietary protein with longitudinal insulin resistance, prediabetes and type 2 diabetes: The Rotterdam study. *Clin. Nutr.* **39**(1), 242–249 (2020).
47. Hernández, E. Á. et al. Acute dietary fat intake initiates alterations in energy metabolism and insulin resistance. *J. Clin. Investig.* **127**(2), 695–708 (2017).
48. Villegas, R., Salim, A., Flynn, A. & Perry, I. Prudent diet and the risk of insulin resistance. *Nutr. Metab. Cardiovasc. Dis.* **14**(6), 334–343 (2004).
49. Chuang, S.-C. et al. Dietary inflammatory patterns are associated with serum TGs and insulin in adults: A community-based study in Taiwan. *J. Nutr.* **153**(6), 1783–1792 (2023).
50. Glass Christopher, K. & Olefsky, J. M. Inflammation and lipid signaling in the etiology of insulin resistance. *Cell Metab.* **15**(5), 635–645 (2012).
51. Randle, P. J., Garland, P. B., Hales, C. N. & Newsholme, E. A. The glucose fatty-acid cycle. Its role in insulin sensitivity and the metabolic disturbances of diabetes mellitus. *Lancet* **1**(7285), 785–789 (1963).

Acknowledgements
Authors have no acknowledgments to declare.

Author contributions
Conceptualization, ZY and AH; Formal analysis, ZY; Methodology, VB, MB, MC, MST and AS; Project administration, MC and AH; Writing—original draft, MC, MST and ZY; Writing—review and editing, ZY and AH. All authors read and approved.

Declarations

Competing interests
The authors declare no competing interests.

Ethics approval and consent to participate
The study was approved by the Research Ethics Committee of Shahid Beheshti Medical University of Iran, under protocol number IR.SBMU.RETECH.REC.1402.689. All participants provided written informed consent and were informed about the study. All procedures performed in studies involving human participants adhered to the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Additional information
Correspondence and requests for materials should be addressed to A.H. or Z.Y.