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The Association of Dietary Inflammatory Index with the Risk of Peptic Ulcer: A Case-Control Study

Faezeh Fouladvand; MSc[1], Mehdi Birjandi; PhD[2], Sadegh Amiri Kia; BSc[3] & Ebrahim Falahi; PhD[*4,5]

[1] Student Research Committee, Lorestan University of Medical Sciences, Khorramabad, Iran; [2] Department of Biostatistics and Epidemiology, Lorestan University of Medical Sciences, Khorramabad, Iran; [3] Endoscopy Department of Shahid Rahimi Hospital, Lorestan University of Medical Sciences, Khorramabad, Iran; [4] Nutritional Health Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran; [5] Department of Nutrition, Lorestan University of Medical Sciences, Khorramabad, Iran..

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Corresponding author:
falahi.e@lums.ac.ir
Nutrition Department, School of Health and Nutrition, Lorestan University of Medical Sciences, Khorramabad, Iran.

Postal code: 6819789741
Tel: +98 916 6616711

ABSTRACT

Background: Peptic ulcer disease (PUD) is a gastrointestinal ulcer caused by gastric acid. Aging, smoking and alcohol, stressful life, and family history are directly related to PUD. Oxidative stress and inflammation are the most important mechanisms involved in PUD. The aim of this study is to evaluate the association of dietary inflammatory index (DII) with the risk of PUD. **Methods:** In this case-control study, data from 100 newly diagnosed peptic ulcer patients and 150 healthy individuals were analyzed. DII was assessed based on dietary intake data collected through a 174-item validated food frequency questionnaire (FFQ). To calculate DII, 36 nutrients and food components were used after adjusting the energy intake. Adjusted odds ratios (OR) and 95% confidence intervals (CI) regarding the association between DII and PUD risk were estimated by logistic regression. **Results:** The mean DII score in patients (0.43±1.88) was significantly higher than the mean DII in healthy individuals (-2.88±2.00) (P=0.005), i.e. patients had received more inflammatory diet. In the crude model of PUD, odds increased significantly in the third and fourth quartiles of DII score compared to the lowest quartile (OR of third quartile vs first quartile: 2.65, 95% CI:1.27-5.52, respectively; and OR of fourth quartile vs first quartile: 2.33, 95% CI:1.12-4.85, respectively; *P-trend*=0.001). After checking multiple potential confounders, OR in third and fourth quartiles remained high and there was no change in the results. **Conclusions:** These findings suggest that more pro-inflammatory diets, indicated by higher DII scores, may increase the risk of PUD. Therefore, anti-inflammatory diet may play a protective role against PUD.

Keywords: *Dietary inflammatory index; Peptic ulcer*

Introduction

Peptic ulcer disease (PUD) is a gastrointestinal ulcer caused by gastric acid and is associated with damage to the gastric mucosa and submucosa of the stomach and duodenum. It occurs when the balance between aggressive factors such as stomach acid and free radicals and defense factors such as gastric mucus and antioxidant defenses is disturbed. Oxidative stress and inflammation are the most important mechanisms involved in gastric ulcer (Narayanan *et al.*, 2018, Sayehmiri *et al.*, 2018, Tarasconi *et al.*, 2020).

The prevalence of gastric ulcer in general

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population of the world is estimated at 6-15%, which is decreasing; but in Iran, the prevalence is estimated at 34%, (30% in women and 60% in men). In general, the prevalence of the disease in Iran is higher than the global rate and is increasing (Abebaw *et al.*, 2017, Sung *et al.*, 2009).

Aging, smoking and alcohol, stressful life, and family history are directly related to PUD. Taking nonsteroidal anti-inflammatory drugs (NSAIDs) and Helicobacter pylori infection are the most important risk factors (Bandyopadhyay *et al.*, 2001, Kuna *et al.*, 2019). Lifestyle factors such as obesity, inactivity, and dietary factors such as poor nutrition, unhealthy diets, and excessive coffee intake are associated with the disease. Studies show that various fruits and vegetables fight PUD through anti-inflammatory, antioxidant, anti-secretory, antimicrobial, anticholinergic, and cellular defense mechanisms. Moreover, phytochemicals in fruits and vegetables play a vital role in prevention and treatment of disease (Harsha *et al.*, 2017, Milosavljevic *et al.*, 2011, Rajagopal *et al.*, 2018).

Some studies demonstrated that reactive oxygen species induced by oxidative stress in the gastric system activate inflammatory responses associated with gastric injury and ulceration. During inflammation, different cytokines and inflammatory mediators are secreted by gastric mucosa. Increased production of multifunctional pro-inflammatory and pro-cytokines such as (TNF-α), IL-1β, IL-6, IL-8, as well as the involvement of COX-2 in response to inflammatory mediators, play an important role in pathogenesis of gastric ulcers (Rajagopal *et al.*, 2018).

Diets rich in fruits, vegetables and antioxidants reduce systemic inflammation, and conversely, diets rich in red and processed meats, fried foods, desserts and sweets are associated with increased inflammation (Mu *et al.*, 2017). DII evaluates inflammatory potential of the diet based on the pro-inflammatory and anti-inflammatory properties of various food compounds, including macronutrients, micronutrients, and certain specific food compounds (Khosravi *et al.*, 2015, Ozawa *et al.*, 2017).

High DII is associated with an increased risk of diseases such as cardiovascular disease, metabolic syndrome, various cancers including gastric and colorectal cancer, and an increase in inflammatory markers (Cavicchia *et al.*, 2009, Fowler and Akinyemiju, 2017, Garcia-Arellano *et al.*, 2015, Kim *et al.*, 2018, Shivappa *et al.*, 2014a, Vahid *et al.*, 2017, Wang *et al.*, 2018).There have been no studies on the association between DII and PUD risk; and this is the first study in this field. This research aims to investigate the relationship between DII and the risk of PUD.

Materials and Methods

Study design and participants: This hospital-based case-control study was conducted in west of Iran from July 2019 to May 2020.The sample size consisted of 250 people, 100 in the case group (patients with PUD) and 150 in the control group (healthy persons). PUD was diagnosed endoscopically by a gastroenterologist. Only patients diagnosed with PUD in the last 6 months were included in the study. Case and control participants were selected by sequential sampling method and were matched on sex. Inclusion criteria included following items: a) the age range of 18-65 years, b) patients recently diagnosed (≤6 months), c) the absence of conditions such as pregnancy and lactation, d) no inflammatory diseases such as rheumatoid arthritis, diabetes, cardiovascular disease and cancer, e) providing informed consent. Exclusion criteria consisted of : a) following a special diet, b) failure to complete the questionnaire, and c) not providing informed consent

Measurements: A semi-quantitative food frequency questionnaire (FFQ) with 174 items was used to examine food intake. A standard size for each type of food was designed based on Willett method (Willett, 2012). The validity and reliability of FFQ were previously confirmed and reported (Haghighatdoost *et al.*, 2015, Mirmiran *et al.*, 2010). In this questionnaire, individuals were asked about the frequency of consumption of each food item during the past year. Depending on the type of food consumed, the frequency of

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consumption per day, week, month, or year was questioned. The amounts reported for each type of food by individuals were converted to grams per day using the Home Scale Handbook. Finally, the exact amount of energy, micronutrients, and macronutrients received by each individual was calculated using the Nutritionist IV software.

To calculate DII score, food assessment data were used. The validated method proposed by Shivappa was used to calculate DII (Shivappa *et al.*, 2014b). Before calculating DII, the received values were adjusted by Residual method based on the received energy (Willett *et al.*, 1997). Some of the food items which needed to calculate DII were not measurable; therefore, only 36 items were used: energy, carbohydrates, protein, total fat, monounsaturated fatty acids, polyunsaturated fatty acids, saturated fatty acids, cholesterol, omega-3, omega-6, fiber, thiamine, riboflavin, niacin, vitamin B6, folic acid, vitamin B12, vitamin A, vitamin C, vitamin E, vitamin D, iron, beta-carotene, selenium, zinc, magnesium, caffeine, tea, garlic, onion, saffron, ginger, turmeric, pepper, thyme and rosemary.

All participants were asked questions about age, sex, education, occupation, monthly household income, marital status, history of smoking, alcohol, history of NSAIDs, supplement intake, and family history of PUD.

The severity of symptoms of depression, anxiety, and stress was measured by DASS-21. DASS (depression, anxiety, and stress) scale is a set of three self-report scales to assess negative emotional status in depression, anxiety, and stress. This questionnaire evaluates 7 cases for each of the three states. It measures 21 items. The validity and reliability of this questionnaire in the Iranian population has been confirmed in several studies (Cronbach's alpha 0.81 to 0.98) (Jafari *et al.*, 2017, Samani and Joukar, 2007).

Physical activity assessment was performed using the abbreviated form of International Physical Activity Questionnaire (IPAQ) (23).

Weight was measured using a standard and calibrated Beurer PS07 scale made in Germany with an accuracy of 100 grams. A person's weight was measured with minimal clothing and no shoes. Then, using a height gauge with an accuracy of 0.1 cm, the standing height of the participant was measured; the individual was without shoes, his/her neck was straight and he/she was looking straight ahead. Waist circumstance was measured using an inelastic tape measure in the smallest area below the chest and above the navel. Hip circumference was measured with the same meter at the largest area. All measurements were performed by the same person.

Ethical considerations: After providing verbal and written explanations about the methodology of the study, informed consent was received from all participants. Participants were allowed to leave the study if they did not want to cooperate. The study protocol was approved by the local Ethics Committee at Lorestan University of Medical Sciences, Khorramabad, Iran and registered with the Code of Ethics: IR.LUMS.REC.1398.05.

Data analyses: General characteristics of the participants were examined between case and control groups using independent sample t-test, Chi-square, and Mann-Whitney U tests. The characteristics of the study participants across quartiles of DII score were presented as means ± SD for continuous variables and percentage for categorical variables. The differences across quartiles were assessed by ANOVA for continuous variables and Chi-square test for categorical variables. ANOVA was used for comparing energy-adjusted dietary intakes of participants across quartiles of DII score. The relationship between the trend of DII quartiles and PUD was studied by modulating different variables. For this purpose, logistic regression was used for calculation of OR and 95% CI in crude and multivariable adjusted models. In the first model, age and energy intake were adjusted. In the second model, in addition to age and energy intake, stress, anxiety, depression, physical activity, smoking, supplements and NSAID intake were adjusted. SPSS20 was used in all analyses and P-value lower or equal 0.05 was considered statistically significant.

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Results

The general characteristics of the participants are presented in **Table 1**. Cases were significantly older and had larger waist circumference and waist-to-hip ratio than those in control group. In contrast, the amount of physical activity in the control group was significantly higher than the case group. There was no significant difference between the two groups regarding weight, height, BMI, and hip circumference. DII score was in the range of -5.53 to 5.47 with a median of 0.13, the mean and standard deviation of -2.88±2.00 in the control group and 0.43±1.88 in the case group. There was a significant difference between the two groups (P=0.005). This indicated that people in the case group received a more pro-inflammatory diet.

The results of univariate analysis suggested that there was a significant difference between case and control groups regarding qualitative characteristics including marital status, education, income, smoking, alcohol, NSAID, supplements intake, family history of disease, level of physical activity, and stress and depression (P<0.05). There was no significant relationship between occupation, anxiety level, and PUD (**Table 2**).

Table 3 compares the mean of nutrient intake between the case and control groups. The results showed that there was a significant difference only between the mean fiber intake of the case group 17.94±6.60 and the control group 21.20±5.67 g/day (P<0.001). There was no significant difference between energy, carbohydrate, protein, fat, cholesterol, saturated fat, MUFA and PUFA intake in case and control groups.

DII score was divided into four quartiles: ≤-1.35 (first quartile), from -1.35 to 0.13 (second quartile), from 0.13 to 1.5 (third quartile), and >1.5 (fourth quartile). General characteristics of participants were compared in quartiles. Compared with those in the lowest DII quartile, participants in the highest DII quartile, had smaller BMI and hip circumference and less physical activity, and were mostly males with low education level. (**Table 4**)

Table 5 compares the average intake of 36 food items in DII quartiles. The mean intake of omega-3, iron, magnesium, zinc, selenium, vitamin A, beta carotene, vitamin E, riboflavin, vitamin B6, folic acid, vitamin C, vitamin D, fiber and foods including garlic, onion, saffron, ginger, turmeric, and pepper were significantly higher in the lowest DII quartile than in the highest DII quartile (P<0.05). There was no significant difference between other variables in DII quartiles.

The relationship between the trend of DII quartiles and PUD was studied by modulating different variables (**Table 6**). The results of the crude model revealed that with increasing DII quartiles, the odds of developing PUD increased (P-*trend*=0.001). The odds of PUD were 28% lower in the second DII quartile than in the first DII quartile, but this relationship was not significant (0R: 0.72; 95% CI: 0.33-1.60). However, the odds of PUD in the third and fourth DII quartiles were significantly higher than the first (the third quartile OR: 2.65; 95% CI: 1.27-5.52 and the fourth quartile OR: 2.33; 95% CI: 1.12-4.85). In the first model, after adjusting the age and the amount of energy intake, a similar result was obtained with the previous part, so that with increasing DII quartiles, the odds of PUD increased (P-*trend*=0.002); the highest odds of PUD were observed in the third quartile (OR: 3.47; 95% CI: 1.52-7.90). In the second model, adding stress, anxiety, depression, physical activity, body mass index, smoking, supplements and NSAID intake to the previous model did not change the overall result (P-*trend*=0.001); the highest odds of PUD were observed in the third quartile (OR: 3.80; 95% CI: 1.40-10.33).

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Table 1. Comparison of general variables between case and control groups.

Variables	Control group (n=150)	Cases group (n=100)	P-value[a]
Age (year)	35.69±11.12[b]	47.75±15.82	<0.001
Weight (kg)	74.16±12.78	74.72±15.37	0.755
Height (m)	1.70±0.09	1.71±0.08	0.646
Body mass index (kg/m^2)	25.46±4.15	25.39±4.30	0.898
Waist circumference (cm)	88.62±10.79	91.85±11.76	0.027
Hip circumference (cm)	102.01±7.80	101.71±6.81	0.749
Waist to hip ratio	0.86±0.07	0.9±0.08	0.001
Physical activity (Met-min/week)	2033.89±1492.84	1348.39±1393.16	<0.001
Dietary inflammatory score	-2.88±2.00	0.43±1.88	0.005

[a]: Independent sample *t-test*; [b]: Mean±SD.

Table 2. Consensus table of subjects in terms of qualitative variables in case and control groups

Variables	Categories	Control group (n=150)	Case group (n=100)	P-value[a]
Sex	Female	57 (38.0)[b]	35 (35.0)	0.689
	Male	93 (62.0)	65 (65.0)	
Marital status	Married	104 (69.4)	85 (85.0)	<0.001
	Single	46 (30.6)	15 (15.0)	
Education	Illiterate	5 (3.4)	22 (22.0)	<0.001
	Diploma or less	93 (62.0)	50 (50.0)	
	Higher than diploma	52 (34.6)	28 (28.0)	
Occupation	Unemployed	51 (34.0)	27 (27.0)	0.059
	Employee	13 (8.7)	15 (15.0)	
	Manual worker	23 (15.3)	21 (21.0)	
	Self-employment	63 (42.0)	37 (37.0)	
Income (Toman)	<2 millions	74 (49.3)	35 (35.0)	0.041
	2-4 millions	63 (42.0)	55 (55.0)	
	>4 millions	13 (8.7)	10 (10.0)	
Smoking	No	134 (89.3)	74 (74.0)	0.001
	Yes	14 (9.3)	16 (16.0)	
	Has quit	2 (1.3)	10 (10.0)	
Alcohol	No	149 (99.3)	92 (92.0)	0.008
	Yes	1 (0.7)	4 (4.0)	
	Has quit	0 (0.0)	4 (4.0)	
Nonsteroidal anti-inflammatory drugs	No	138 (92.0)	74 (74.0)	<0.001
	Yes	12 (8).0	26 (26.0)	
Supplement	No	133 (88.7)	98 (98.0)	0.006
	Yes	17 (11.3)	2 (2.0)	
Family history	No	138 (92.0)	75 (75.0)	<0.001
	Yes	12 (8.0)	25 (25.0)	
Stress	Normal	108 (72.0)	52 (52.0)	0.005
	Light	15 (10.0)	22 (22.0)	
	Medium	13 (8.7)	15 (15.0)	
	Intense	10 (6.7)	9 (9.0)	
	Very intense	4 (2.7)	2 (2.0)	
Anxiety	Normal	102 (68.0)	74 (74.0)	0.173
	Light	19 (12.6)	14 (14.0)	
	Medium	8 (5.3)	8 (8.0)	
	Intense	7 (4.7)	2 (2).0	
	Very intense	14 (9.3)	2 (2.0)	

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Table 2. Consensus table of subjects in terms of qualitative variables in case and control groups

Variables	Categories	Control group (n=150)	Case group (n=100)	P-value[a]
Depression	Normal	109 (72.7)	85 (85.0)	0.013
	Light	9 (6.0)	7 (7.0)	
	Medium	21 (14.0)	6 (6.0)	
	Intense	4 (2.7)	1 (1.0)	
	Very intense	7 (4.7)	1 (1.0)	

[a]: Chi-square *test*; [b]: N (%).

Table 3. Comparison mean of daily intake of energy and nutrients between case and control groups.

Variables	Controls (n=150)	Cases (n=100)	P-value[a]
Energy (kcal/day)	2811.52±733.90[b]	2837.19±990.88	0.825
Carbohydrate (g/day)	411.67±112.36	405.4±144.31	0.715
Protein (g/day)	105.95±30.98	105.43±41.98	0.916
Fiber (g/day)	21.20±5.67	17.94±6.60	<0.001
Fat (g/day)	88.82±32.17	93.32±42.70	0.371
Cholesterol (mg/day)	333.95±209.57	335.19±255.04	0.967
Saturated fatty acid (g/day)	24.66±10.97	26.40±14.60	0.313
Mono unsaturated fatty acid (g/day)	29.01±10.73	32.10±14.16	0.065
Poly unsaturated fatty acid (g/day)	19.10±8.63	20.03±10.07	0.459

[a]: Independent sample *t-test*; [b]: Mean±SD.

Table 4. Comparison mean of quantitative variables of participants between different DII quartiles.

Variables	Q1	Q2	Q3	Q4	P-value[a]
	DII≤-1.35	-1.35<DII<0.13	0.13<DII<1.5	DII>1.5	
Age (year)	40.6±12.25[b]	38.15±13.9	40.4±15.35	42.89±15.9	0.339
Weight (kg)	75.93±13.79	73.12±13.78	72.43±12.45	76.05±15.18	0.329
Height (m)	1.68±0.1	1.7±0.08	1.71±0.09	1.73±0.08	0.042
Body mass index (kg/m^2)	26.77±4.71	25.12±4.04	24.57±3.56	25.3±4.22	0.025
Waist circumference (cm)	92.2±10.97	88.69±10.57	87.87±11.21	90.9±12.03	0.119
Hip circumference (cm)	104.83±8.65	101.29±5.95	100.41±6.01	101.07±7.99	0.003
Waist to hip ratio	0.87±0.07	0.87±0.07	0.87±0.08	0.89±0.07	0.295
Physical activity (Met-min/week)	2054±1588	1392±1425	1971±1557	1619±1310	0.045

[a]: ANOVA test; [b]: Mean±SD; Q1:First quartile; Q2: Second quartile; Q3: Third quartile; Q4: Fourth quartile..

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Table 5. Comparison of food items between participants in DII quartiles.

Variables	Q1	Q2	Q3	Q4	P-value[a]
	DII≤-1.35	-1.35<DII<0.13	0.13<DII<1.5	DII>1.5	
Energy (kcal/day)	2880.69±896.37[b]	2611.76±814.79	2927.55±838.44	2086.77±809.53	0.152
Protein (g/day)	109.38±37.08	99.51±33.76	109.74±37.07	104.29±34.67	0.332
Carbohydrate (g/day)	415.36±131.13	371.80±113.71	428.54±134.2	420.46±118.49	0.054
Fat (g/day)	94.9±38.87	87.20±36.61	91.01±32.71	89.39±38.89	0.695
Cholesterol (mg/day)	337.96±212.63	319.2±162.29	349.34±230.97	331.09±291.87	0.904
Saturated fatty acid (g/day)	25.92±12.45	24.64±12.92	25.64±11.78	25.23±13.26	0.948
Mono unsaturated fatty acid (g/day)	30.16±11.69	28.33±12.03	30.79±11.37	31.68±13.93	0.479
Poly unsaturated fatty acid (g/day)	21.40±10.00	18.64±10.12	19.34±7.98	18.57±8.59	0.282
Omega-6 (g/day)	17.9±8.80	16.37±9.76	16.54±7.61	16.26±8.08	0.655
Omega-3 (g/day)	0.40±0.24	0.32±0.15	0.40±0.25	0.25±0.12	<0.001
Iron (mg/day)	23.86±6.71	20.27±6.41	22.29±7.07	21.16±7.19	0.025
Magnesium (mg/day)	369.56±127.92	287.4±81.04	293.12±114.95	240.57±100.69	<0.001
Zinc (mg/day)	12.56±4.76	11.03±4.19	11.44±4.41	10.07±4.44	0.02
Selenium (µg/day)	130.00±50.00	100.00±40.00	100.00±40.00	90.00±50.00	<0.001
Vitamin A (RE)	1827.77±1236.35	1244.52±879.10	1106.82±806.65	740.34±529.83	<0.001
Beta carotene (µg/day)	831.52±1039.36	379.15±415.04	299.14±350.45	133.40±121.48	<0.001
Vitamin E (mg/day)	5.88±3.17	4.37±2.14	4.83±3.40	3.14±11.53	<0.001
Thiamin (mg/day)	2.64±0.83	2.33±0.67	2.66±0.78	2.59±0.74	0.061
Riboflavin (mg/day)	2.48±1.06	2.07±0.81	2.18±0.87	1.84±0.77	0.001
Niacin (mg/day)	29.08±10.32	26.92±9.90	30.82±10.1	30.22±9.18	0.134
Vitamin B6 (mg/day)	2.25±1.00	1.81±0.78	1.76±0.77	1.39±0.69	<0.001
Folic acid (µg/day)	375.17±111.02	101.76±294.78	262.21±80.47	221.92±78.89	<0.001
Vitamin B12 (µg/day)	7.57±6.84	7.28±8.21	6.93±6.68	5.60±5.83	0.398
Vitamin C (mg/day)	151.19±56.83	104.93±32.24	93.98±26.27	75.02±21.66	<0.001
Vitamin D (µg/day)	1.57±1.39	0.92±0.94	1.05±0.91	0.82±1.15	0.001
Fiber (g/day)	25.07±5.21	19.66±5.09	18.48±5.91	16.45±5.40	<0.001
Caffeine (g/day)	0.216±0.15	0.18±0.11	0.19±0.14	0.17±0.13	0.381
Tea (g/day)	996.62±732.38	850.78±586.13	837.46±708.01	730.46±608.96	0.168
Garlic (g/day)	2.08±3.20	0.65±0.93	0.82±2.08	0.61±1.32	<0.001
Onion (g/day)	36.01±26.74	33.70±29.31	24.00±23.88	21.44±25.57	0.004
Saffron (g/day)	0.01±0.04	0.00±0.00	0.00±0.00	0.00±0.00	0.005
Ginger (g/day)	0.33±0.73	0.11±0.23	0.09±0.32	0.08±0.29	0.004
Turmeric (mg/day)	2176.03±1497.92	1791.47±1161.20	1485.63±901.46	1277.77±724.51	<0.001
Pepper (g/day)	0.59±0.96	0.18±0.41	0.14±0.33	0.11±0.21	<0.001
Rosemary (mg/day)	5.22±25.56	25.84±165.05	7.19±54.03	00.00±00.00	0.379
Thyme (mg/day)	490.19±764.47	341.32±843.10	197.31±467.47	248.88±615.43	0.09

[a]: ANOVA test; [b]: Mean±SD; Q1:First quartile; Q2: Second quartile; Q3: Third quartile; Q4: Fourth quartile..

Table 6. Relationship between the trend of DII score quartiles with peptic ulcer disease with modulation of confounding factors using logistic regression model.

Variables	DII≤-1.35	-1.35<DII<0.13	0.13<DII<1.5	DII>1.5	P-Trend
Crude model	reference	0.72 (0.33-1.60)[a]	2.65 (1.27-5.52)	2.33 (1.12-4.85)	0.001
Model I[b]	reference	0.94 (0.39-2.26)	3.47 (1.52-7.90)	2.75 (1.18-6.40)	0.002
Model II[c]	reference	0.61 (0.21-1.82)	3.80 (1.40-10.33)	3.09 (1.12-8.56)	0.001

[a]: Data are presented as odds ratio (OR) and confidence interval of 0.95 (95% CI); [b]: Model I: adjusted based on age and energy; [c]: Model II: Model 1 and stress, anxiety, depression, physical activity, body mass index, smoking, supplements and NSAIDs intake adjustment; DII: Dietary inflammatory score..

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Discussion

In the present study, the age of the patients with PUD was significantly higher than the control group; but, there was no significant difference between the subjects in different DII quartiles. Aging and the accompanying defects in apoptosis, angiogenesis, and sensory nerve activity predisposes individuals to gastric mucosal damage, which in the current study was associated with an increased risk of PUD (Teshome *et al.*, 2019). There was no significant difference between weight and BMI in case and control groups; however, the WHR of patients was significantly higher than the control group. Other studies have shown a positive association between weight, BMI, general obesity, and central obesity and the increased risk of PUD, especially gastric ulcers and negative Helicobacter pylori ulcers (Boylan *et al.*, 2014, Kim *et al.*, 2017). Previous studies have shown that pro-inflammatory diet and higher DII score were associated with higher weight and BMI (Kim *et al.*, 2017). However, in the present study, despite higher DII in patients, there was no significant difference in their weight compared to healthy individuals. There was no significant difference in energy intake between case and control groups and between DII score quartiles. In line with a pervious study, the physical activity of the cases was significantly lower than the control group. Moreover, participants in the higher DII quartiles had significantly less physical activity (Paik *et al.*, 2020). Physical activity could possibly affect PUD through several biologic mechanisms, including enhancing the immune system's ability to neutralize the effects of H pylori, reducing excess acid secretion, and improving a person's ability to cope with stressful situations (Cheng *et al.*, 2000). Moreover, smoking, alcohol, NSAID intake, and family history were significantly higher in the case group than the control group. In the present study, the results showed that stress intensity was higher in the case group compared with the control group. Smoking increased basal gastric acid secretion through stimulation of H2-receptor by histamine release and decreased the secretion of epidermal growth factor from the salivary gland, which is necessary for gastric mucosal cell renewal. Alcohol consumption increases gastric acid secretion by maleic and succinic acids and causes mucosal damage and disruption which increases mucosal acid permeability (Kurata and Nogawa, 1997, Teshome *et al.*, 2019). Taking NSAID destroys the gastric mucosa and increases the risk of ulcers and bleeding (Shim *et al.*, 2019). The digestive system is vulnerable to the influence of emotional factors, because its function is regulated mainly by vegetative nervous system and endocrine system; the center of both systems has the same anatomical location as the subcortical integration center of the emotional center (Zhang *et al.*, 2016). Stress, anxiety and depression can affect the spread of gastric ulcers by affecting biological mechanisms such as blood flow and gastric acid secretion (Deding *et al.*, 2016). In the case group, compared with the control group, fiber consumption was significantly lower. Higher fiber intake was associated with lower plasma levels of pro-inflammatory factors such as CRP, IL-6, and receptor 2 of the TNF-α; there is evidence regarding interactions between dietary fiber and gut microbiota composition in the pathogenesis of inflammation by impairing intestinal barrier function and increasing permeability (Ma *et al.*, 2021). Despite receiving more calories, fat, saturated fat, cholesterol, MUFA and PUFA, these differences were not significant. Furthermore, there was no significant difference between the two groups in terms of carbohydrate and protein intake. The study by Elmstahl *et al.* also showed that fiber consumption in patients was lower than healthy individuals, but unlike this study, the consumption of total fat, saturated fat, and monounsaturated fatty acids in them was higher than the control group (Elmstahl *et al.*, 1998). Various studies have indicated the anti-inflammatory properties of omega-3 (Gutiérrez *et al.*, 2019), zinc (Olechnowicz *et al.*, 2018), magnesium (Hu *et al.*, 2018), selenium (Ibrahim *et al.*, 2019), vitamin A (Caram *et al.*, 2015), beta carotene (Kawata *et al.*, 2018), vitamin E (Lewis *et al.*, 2019), vitamin B6 (Shan *et al.*, 2020), folic acid (Huang *et al.*, 2016), vitamin C (Bowie and

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O'Neill, 2000), vitamin D (Rai *et al.*, 2016), and riboflavin (Mazur-Bialy and Pocheć, 2016). The anti-inflammatory properties of fiber, garlic, onion, saffron, ginger, pepper, and turmeric were observed in various studies (Ansary *et al.*, 2020, González-Peña *et al.*, 2017, Hatziagapiou *et al.*, 2019, He *et al.*, 2015, Jolayemi and Ojewole, 2013, Lie *et al.*, 2018, Mohd Sahardi and Makpol, 2019). Based on the findings of the present study, the intake of these food items was significantly higher in lower quartiles of DII than the higher quartiles. Inflammation plays an important role in the development of peptic ulcer, and in one study, drinking hot tea was associated with the disease (Nemati *et al.*, 2012). However, there was no significant difference between inflammatory quartiles regarding caffeine and tea consumption. It can be seen that these two food items probably had no effect on inflammation and ultimately on the disease. In two studies which examined the association between DII and gastric cancer risk, a positive association was found between increased DII scores and the disease risk, which is associated with the role of pro-inflammatory diets with insulin resistance and increased systemic inflammation (Lee *et al.*, 2017, Vahid *et al.*, 2018). Various studies have shown that the inflammatory potential of diet due to high intake of salty foods and red meat increases the risk of gastric cancer, and conversely, high intake of fruits and vegetables and vitamin C reduces the risk of gastric cancer. Moreover, Western or unhealthy diet patterns increased the risk compared to healthy diet patterns. In general, the spread of chronic inflammation due to chronic atrophic gastritis, metaplasia, or intestinal dysplasia can lead to gastric cancer, and controlling chronic gastritis by diet helps prevent disease progression (Correa *et al.*, 1975, Lee *et al.*, 2017, Moss and Blaser, 2005). Overall, this is the first study to examine the association of DII with the risk of PUD and the latest version of the method of Shivappa with 36 items was used for calculation; but, other items were not available for DII calculation, and a calculation error is possible due to an error in the diet reception reports. Since patients were enrolled in the study up to 6 months after diagnosis, there was a possibility of error in recalling dietary intakes and weight loss at this time; this was the result of examining the relationship between anthropometric indices and the risk of disease with non-significant results.

Conclusions

In general, a pre-inflammatory diet with a higher score of DII is associated with an increased risk of PUD. An anti-inflammatory diet with a lower DII score, more physical activity, reduced waist size, stress controlling, avoiding of NSAID, smoking and alcohol is recommended for all people as a solution to prevent PUD. It is necessary that more studies confirm the results of these study. More reliable results can be obtained if a prospective study with a high sample size is performed using 24-hour food recall in addition to the FFQ to examine the plasma levels of inflammatory factors.

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Conflict of interest

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Authors' contributions

Falahi E designed and supervised the study; Fouladvand F sampled and collected data and calculated DII; Amir Kia S conducted diagnosis of disease and sampling; Birjandi M analyzed and interpreted data; Fouladvand F write the main manuscript all the tables; Birjandi M corrected and revised the statistical analyses and results; Falahi E write and discussed and reviewed the article. All authors approved of the final manuscript.

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