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PANCREATITIS IN GALLSTONE PATIENTS: IS THERE ANY LINK BETWEEN DIET AND DISEASE?

SAFRA TAŞI HASTALARINDA PANKREATİT: DİYET İLE HASTALIK ARASINDA BİR BAĞLANTI VAR MI?

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ABSTRACT

Objective: Acute pancreatitis is most often caused by gallstones. There is no clear relationship between diet and gallstone pancreatitis. The purpose of this research was to examine dietary differences in pancreatitis patients with gallstones.

Material and Method: Patients with acute biliary pancreatitis and patients with gallstones without pancreatitis were included in this prospective case-control study. Groups were set to be similar in case numbers, age, gender, and gallbladder stone size. A three-day food consumption questionnaire and a food consumption frequency questionnaire were applied to all volunteers. The BeBis 8 Full version program was used to evaluate body mass index, alcohol and cigarette consumption status, daily physical activity status, eating frequency, and food consumption status.

Result: A total of 120 patients, including 60 patients who developed pancreatitis due to gallstones, and 60 patients who only had gallstones were included in the study. Among the demographic data, monthly income was statistically higher in pancreatitis. In addition, it was found that the daily milk-yoghurt, red meat, chicken, salami-sausage, egg, rice-pasta, protein, fat, and cholesterol intakes of patients with pancreatitis were significantly higher. In the multivariate logistic regression analysis, it was determined that the increase in daily milk-yoghurt, egg, rice-pasta and protein intake were independent risk factors.

Conclusion: Reducing the consumption of red meat, eggs, fat, cholesterol, milk-yoghurt, rice and pasta, salami and sausage in people with gallstones may reduce the incidence of acute pancreatitis in these individuals.

Keywords: Gallstone, pancreatitis, diet, red meat, egg

ÖZET

Amaç: Akut pankreatiti genellikle safra taşlarından kaynaklanır. Diyet ile safra taşı pankreatit arasında net bir ilişki bulunmamaktadır. Bu araştırmanın amacı, safra taşı olan pankreatit hastalarında beslenme farklılıklarını incelemektir.

Gereç ve Yöntem: Bu prospektif vaka-kontrol çalışmasına akut biliyer pankreatiti olan hastalar ve pankreatit gelişmemiş safra taşı olan hastalar dahil edilmiştir. Gruplar, vaka sayıları, yaş, cinsiyet ve safra kesesi taşı büyüklüğü açısından benzer olarak belirlendi. Tüm gönüllülere üç günlük besin tüketim formu ve besin tüketim sıklığı formu uygulandı. Vücut kütle indeksi, alkol ve sigara tüketimi durumu, günlük fiziksel aktivite durumu, yeme sıklığı ve besin tüketim durumunu değerlendirmek için BeBis 8 Full versiyon programı kullanıldı.

Bulgular: Çalışmaya, safra taşları nedeniyle pankreatit gelişen 60 hasta ve pankreatit gelişmemiş safra taşı olan 60 hasta olmak üzere toplam 120 hasta dahil edildi. Demografik veriler arasında aylık gelir pankreatit gelişenlerde istatistiksel olarak daha yüksek bulundu. Ayrıca, pankreatitli hastaların günlük süt-yoğurt, kırmızı et, tavuk, salam-sosis, yumurta, pirinç-makarna, protein, yağ, kolesterol alımlarının anlamlı olarak daha yüksek olduğu tespit edildi. Çok değişkenli lojistik regresyon analizinde, günlük süt-yoğurt, yumurta, pirinç-makarna ve protein alımındaki artışın bağımsız risk faktörleri olduğu belirlendi.

Sonuç: Safra taşı olan bireylerde kırmızı et, yumurta, yağ, kolesterol, süt-yoğurt, pirinç ve makarna, salam ve sosis tüketiminin azaltılması, akut pankreatit insidansını bu kişilerde azaltabilir.

Anahtar Kelimeler: Safra taşı, pankreatit, diyet, kırmızı et, yumurta

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INTRODUCTION

There is an annual incidence of 4.9-35 cases of acute pancreatitis (AP) in every 100,000 people and it increases with the rise of obesity and gallstones (1). Age-related incidence is most prevalent between 30-60, and gender-specific incidence does not differ. Acute pancreatitis is usually caused by gallstones, followed by alcohol and drug abuse and other factors (2).

There is some evidence that diet and obesity contribute to the development of gallstones, although the relationship between AP and diet is not fully understood. Patients with obesity have been reported to have a two-fold increased risk of developing gallstones than a body mass index (BMI) of 20-25 in people of normal weight (3). A number of studies have also demonstrated that gallstone is associated with the consumption of refined carbohydrates and triglycerides in the diet, as well as the reduction of dietary fibre (4).

In the literature, limited information is available about the relationship between diet and AP. Moreover, there is often a lack of clarity in the literature about whether patients with acute, chronic, or recurrent pancreatitis or whether pancreatitis develops due to gallbladder stones. As reported in Sarles' 1973 study, high fat and protein consumption as well as alcohol consumption increase the risk of pancreatitis, not being associated with the etiological cause (5). There have been few studies that examined whether the proteins, fats, and carbohydrates are associated with alcohol-related or gallstone-related AP, or whether mortality is related to AP (6-8).

In addition, coffee, consumption of small amounts of fruit, and increased consumption of freshwater fish and boiled rice are among the other etiological factors accused of diet in the development of AP (9-11). It has also been reported that extremely large meals after prolonged fasting (approximately 2000 kcal) and food allergies are risk factors for AP (12,13).

Although there are studies evaluating the relationship between diet and the development of non-biliary pancreatitis or the formation of gallstones AP the number of studies evaluating the role of diet in patients with gallstones pancreatitis in patients with gallstones is very limited. The aim of this study is to determine diet-related factors that may affect the development of ABP in patients with gallstones.

MATERIAL and METHODS

This case-control study was conducted prospectively between June 2021 and December 2021 following approval from the Local Human Ethics Committee (Date: 02.10.2020, No:2530). In addition to the patients hospitalized with the diagnosis of ABP in the general surgery unit, the patients who underwent cholecystectomy due to gallstones in the general surgery unit in the same period as the control group were included in the study. The study has been registered to ClinicalTrials.gov with the number NCT05142657. Informed consent was obtained from all volunteers.

The ABP group included people between 18 and 80 years old, with gallbladder stones and pancreatitis, while the exclusion criteria were cancer, pregnancy, chronic liver or kidney disease, mechanical icterus, and pancreatitis due to endoscopic retrograde cholangiopancreatography (ERCP). Inclusion criteria for the gallstone group were the same as the pancreatitis group except diagnosed with pancreatitis; exclusion criteria were having pancreatitis history and the other pancreatitis group exclusion criteria. Written consent forms were obtained from all of the volunteers. Patients were evaluated in order of hospitalization, and the study was stopped when there were 60 volunteers who met the inclusion-exclusion criteria in each group (Figure 1).

The ABP was diagnosed if the patient met two of the three criteria (sudden onset of pain in the upper abdomen, increasing pancreatic enzymes threefold or more than normal limits in the serum, detection of oedema and inflammation in the pancreas by imaging methods).

Three-day food consumption record and food consumption frequency form was applied to all volunteers. Additionally, the age, gender, BMI, alcohol consumption and smoking, daily physical activity, and eating frequency were noted. BeBis 8 computer program was used for the food consumption calculations and the data were compared between groups.

Statistical analysis was performed with SPSS 22.0 (IBM, Armonk, NY, USA) software. Descriptive statistics included the mean, standard deviation, and rate for numerical variables. Kolmogorov-Smirnov tests were

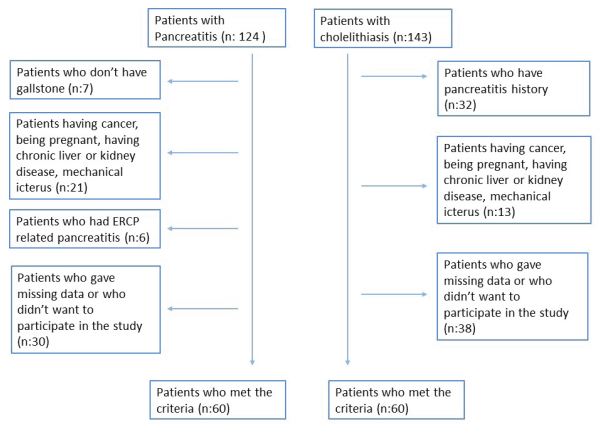

Figure 1: Flow diagram of gallstone cases with and without pancreatitis

used to confirm a normal distribution condition, normally distributed parameters were analysed with the Student T-test and non-normally distributed parameters were analysed with the Mann-Whitney U test. The Chi-Square test was used for categorical variables. Multivariate logistic regression tests were used for the evaluation of the level of impact. The statistical significance level was set at $p<0.05$.

RESULTS

A total of 120 volunteers were included in the study. There are two groups which have 60 patients who developed pancreatitis due to gallstones and 60 patients who only had gallstones and did not develop pancreatitis. The mean age of the volunteers was 53.33±14.90 years and the female/male ratio was 79/41.

When the demographic data, eating and exercise behaviours of the groups were evaluated, it was observed that the monthly income of the patients who had pancreatitis was higher than the patients who did not (p:0.000), and there was no significant difference in other parameters (Table 1).

When the dietary behaviours and food consumption of the participants in the study are evaluated, the intakes of daily milk-yoghurt, daily red meat, daily chicken, daily salami- sausage, daily egg, daily rice-pasta, daily protein, daily fat, daily cholesterol are significantly higher in patients with pancreatitis compared to those who do not. (p=0.006, p=0.019, p=0.000, p=0.043, p=0.000, p=0.000, p=0.000, p=0.029, p=0.015, respectively) (Table 2).

In multivariate logistic regression analyses for pancreatitis, it has been determined that the increase in daily

Table 1: The demographic data and the meal information of the patients according to groups

		Pancreatitis group (n=60)	Gallstone group (n=60)	p value
Gender (n-%)	Female	44 (73.3%)	35 (58.3%)	0.123
	Male	16 (26.7%)	25 (41.7%)	
Age (year±SD)		54.86±18.12	52.81±11.69	0.463
Gallstone size (mm) (median, min-max)		0.75 (0.2-2.4)	0.8 (0.2-2.9)	0.211
BMI (median, min-max)		27.90 (20.80-52.00)	27.69 (22.30-34.40)	0.342
Cigarette (n-%)	No	42 (70.0%)	31 (51.7%)	0.120
	Quit	9 (15.0%)	15 (25.0%)	
	Yes	9 (15.0%)	14(23.3%)	
Alcohol (n-%)	Yes	54 (90.0%)	55 (70.0%)	
	No	6 (10.0%)	5 (91.7%)	
Education level (n-%)	Non-literate	5 (8.3%)	1 (8.3%)	0.752
	Literate	6 (10.0%)	6 (10.0%)	
	Primary school	36 (60.0%)	33 (55.0%)	
	High school	9 (15.0%)	12 (20.0%)	
	University	4 (6.7%)	8 (13.3%)	
Monthly income ($) (n-%)	<150$	6 (10.0%)	30 (50.0%)	**0.000**
	150-300$	38 (63.3%)	20 (33.3%)	
	>300$	16 (26.7%)	19 (16.7%)	
Regular physical activity (at least 30 min/week) (n-%)	Yes	10 (16.7%)	11 (18.3%)	0.810
	No	50 (83.3%)	49 (81.7%)	
Regular breakfast (n-%)	Yes	58 (96.7%)	59 (3.3%)	0.559
	No	2 (98.3%)	1 (1.7%)	
Skipping mean meal in a day (n-%)	Yes	33 (55.0%)	25 (41.7%)	0.144
	No	27 (45.0%)	35 (58.3%)	

BMI: Body mass index, SD: Standard deviation

Table 2: Daily food habits according to pancreatitis existence

	Pancreatitis group (n=60)	Gallstone group (n=60)	p value
Daily milk-yoghurt (ml) (median, min-max)	151.00 (42.90-328.60)	128.55 (0.00-350.00)	**0.006**
Daily cheese (g) (median, min-max)	47.90 (0.00-114.30)	60.00 (5.00-114.30)	0.061
Daily red meat (g) (median, min-max)	21.40 (3.30-57.10)	14.00 (0.00-61.40)	**0.019**
Daily chicken (g) (median, min-max)	57.10 (0.00-128.60)	28.60 (0.00-64.30)	**0.000**
Daily fish (g) (median, min-max)	15.45 (0.00-271.40)	10.00 (0.00-71.40)	0.662
Daily salami-sausage (g) (median, min-max)	9.00 (0.00-85.70)	5.15 (0.00-41.60)	**0.043**
Daily giblets (Liver, kidney etc.) (g) (median, min-max)	0.00 (0.00-84.70)	0.00 (0.00-42.80)	0.850
Daily egg (g) (median, min-max)	57.10 (0.00-150.00)	28.60 (0.00-100.00)	**0.000**
Daily nuts (g) (median, min-max)	7.50 (0.00-57.10)	4.15 (0.00-41.40)	0.230
Daily legumes (g) (median, min-max)	15.00 (0.00-47.10)	10.00 (0.00-42.80)	0.163
Daily bread (g) (median, min-max)	193.75 (10.70-500.00)	150.00 (3.30-300.00)	0.130
Daily rice-pasta (g) (median, min-max)	100.00 (20.00-342.90)	54.30 (0.00-180.00)	**0.000**
Daily vegetable (g) (median, min-max)	128.60 (0.00-385.70)	126.45 (31.40-368.70)	0.202
Daily fruit (g) (median, min-max)	117.85 (0.00-585.70)	114.30 (0.00-500.00)	0.954
Daily fast food (g) (median, min-max)	21.40 (0.00-114.30)	14.00 (0.00-100.00)	0.672
Daily energy intake (kkal) (median, min-max)	1960.00 (1360.70-2681.00)	1844.45 (1326.90-2681.00)	0.152
Daily carbohydrate (g) (median, min-max)	241.15 (172.10-386.40)	216.85 (151.20-386.40)	0.099
Daily protein (g) (mean±SD)	82.63±19.38	65.50±10.73	**0.000**
Daily fat (g) (mean±SD)	83.22±18.89	76.59±13.43	**0.029**
Daily fibre (g) (mean±SD)	21.01±7.42	19.70±5.03	0.260
Daily cholesterol (mg) (mean±SD)	313.40±117.38	265.42±94.86	**0.015**

g: gram, mg: milligram, SD: Standard derivation

milk-yoghurt, daily egg, daily rice-pasta, and daily protein intake are independent risk factors (p=0.020, p=0.003, p=0.006, p=0.001, respectively) (Table 3).

Table 3: Multivariate regression analysis of variables

	OR	95% CI	p value
Monthly income	0.844	0.217-3.285	0.080
Daily protein	0.899	0.841-0.959	**0.001**
Daily fat	1.037	0.994-1.082	0.097
Daily cholesterol	1.009	1.000-1.018	0.054
Daily milk-yoghurt	0.990	0.981-0.998	**0.020**
Daily red meat	1.013	0.968-1.060	0.569
Daily chicken	0.973	0.946-1.001	0.058
Daily salami-sausage	0.961	0.910-1.015	0.154
Daily egg	0.963	0.940-0.987	**0.003**
Daily rice-pasta	0.976	0.959-0.993	**0.006**

DISCUSSION

Gallstones are the leading cause of pancreatitis. The role of diet in the formation of gallbladder stones is an undeniable fact. There are many studies in the related literature.

Many studies have reported that eggs, red meat, animal fat, animal protein, and dietary cholesterol increase the cholesterol content in bile and increase cholesterol gallstones (14-16). It has been reported in some studies that high-protein diets prevent gallstone formation (17,18). Previous studies have shown that refined sugar, cakes and cakes, and beverages containing sucrose increase the risk of gallstones (19,20).

Low consumption of vegetables and high consumption of fat and meat may contribute to the aetiology and development of AP. The secretion of cholecystokinin is increased when meat or fat is consumed by stimulating

the pancreas. The inflammatory cascade may also be influenced by dietary components that have a role in AP pathogenesis by causing reactive oxygen and nitrogen species (21). The pancreas can be sensitive to oxidative stress if its antioxidant status is imbalanced because of dietary factors. In a study that evaluated the relationship between pancreatitis severity and diet and included patients with AP which developed due to many etiological factors, it was stated that increased meat consumption was an independent risk factor for increased pancreatitis severity (22).

In a study by Setiawan et al. that evaluated the relationship between pancreatitis and diet between 1993 and 1996, a positive relationship was found between red meat consumption and AP due to gallstones. In addition, a relationship was found between the consumption of eggs, saturated fatty acids, and cholesterol and the development of AP due to gallstones. On the contrary, it has been observed that there is a negative relationship between pancreatitis and dietary fibre intake, fruit consumption, and the amount of milk consumed. However, in this study, pancreatitis patients were evaluated among themselves according to their consumption frequency, and it was not evaluated whether it affected the development of ABP (23). A large cross-sectional study from China had a positive association with the risk of acute pancreatitis in a high-meat diet model (24).

There is an increased risk for AP associated with overall and saturated fat intake, but no effect of fibre intake on pancreatitis according to the Iowa Women's Health Study (25). Acute pancreatitis appears to be caused by a combination of gallstones and a prolonged high-fat diet, suggesting diet might play a role as a cofactor in AP's onset, according to a previous systematic review (26). An increased risk of ABP has also been linked to a high-cholesterol diet according to two studies. There is a strong connection between high-fat and cholesterol diets and the development of gallstones, both in animal and human studies (27,28).

Wilson et al. in their study in 1985 evaluated patients with acute pancreatitis due to gallstones and patients who did not develop pancreatitis despite having stones in the common bile duct in terms of daily protein, fat, and carbohydrate intake, and there was no significant difference between the groups (6).

In our study, similar to some studies in the literature, daily protein, red meat, egg, fat, and cholesterol consumption is significantly higher in patients with gallbladder pancreatitis. Although there are publications in the literature suggesting that there is an inverse relationship between fibre intake and milk use and AP, there are also publications that do not show any correlation. In our study, no relationship was found between the development of AP and fibre intake, but a positive relationship was observed between the intake of milk-yoghurt and the development of AP. The relationship between the intake of milk-yoghurt and AP can be explained by the preference for fatty milk and yoghurts in our society. In our study, pancreatitis was observed more frequently in patients with gallstones with a higher monthly income, which can probably be explained by easier access to meat, milk, eggs, etc.

Although there are studies showing that fish consumption protects against pancreatitis not related to the gallbladder, no association was found between fish consumption and pancreatitis risk in other multi-ethnic studies (29). In the same study, an inverse relationship was reported between fish consumption and gallbladder acute pancreatitis in the Caucasian population (23). In our study, no significant difference was observed between groups in terms of fish consumption.

Acute pancreatitis is reported to be associated with smoking (30,31). There is a two fold increase in the risk of non-gallstone-related AP among smokers, but not for gallstone-related AP, according to a Swedish study (31). In our study, no difference was found in smoking rates in patients with AP compared to those with only gallstones.

There are very few studies in the literature evaluating the relationship between rice-pasta consumption and AP. Although a positive correlation was reported between parboiled rice and AP in one of these studies, it is not known whether the cases were related to AP due to gallstones (11). In our study, a positive relationship was found between the consumption of rice-pasta and AP due to gallstones. We think that this is not related to the intake of rice or pasta, but to the intake of a large amount of oil during the cooking of these dishes in our country.

Limitations of this study: the limited number of patients, the history of the patients could not be standardized, and situations that may arise from cultural differences could not be evaluated.

CONCLUSIONS

As a result, our study sought to answer which foods may cause pancreatitis in individuals with gallstones, which have been evaluated in very few articles in the literature, and it may be that the intake of red meat, eggs, fat, cholesterol, and protein, which are thought to play a role in the aetiology of AP, may be important in the development of AP related to gallbladder stones. Although an inverse relationship has been reported between the development of AP and the intake of fibre and milk, especially in the literature, a positive relationship was found between the development of AP and these products in our study, especially due to increased fat intake in milk and rice-pasta products. Paying attention to the consumption of these foods can give satisfactory results in preventing

the development of AP in people with gallstones.

Ethics Committee Approval: This study was approved by Istanbul Training and Research Hospital Clinical Research Ethics Committee (Date: 02.10.2020, No: 2530).

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Author Contributions: Conception/Design of Study- S.D., C.İ.; Data Acquisition- M.M.S., U.O.İ.; Data Analysis/Interpretation- İ.Y.; Drafting Manuscript- S.D., C.İ., M.M.S., U.O.İ., İ.Y.; Critical Revision of Manuscript- C.İ.; Final Approval and Accountability- S.D., C.İ., M.M.S., U.O.İ., İ.Y.

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