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Chili pepper consumption and duration of fissure symptoms onset are associated with perianal fistula development among patients with anal fissure: a case-control study

Khadije Gorgi^{1†}, Zahra Ghanbarzadegan^{1†}, Ali Reza Safarpour^{1*†}, Sara Shojaei-Zarghani^{1*†} and Seyed Vahid Hosseini¹

Abstract

Background Perianal fistula is one of the complications of deepened anal fissure. The present case-control study aimed to assess the risk factors of fissure-associated fistulas due to the limited available evidence.

Methods Patients with fissure-associated fistulas were considered as case, and patients with anal fissure who were undergoing medical treatment without any previous anorectal surgeries were considered as control group. Data were collected through medical records or by directly contacting patients. Risk factors of fissure-associated fistulas were assessed using a multivariable logistic regression analysis.

Results The current study included 119 patients, consisting of 54 cases and 65 controls. There were no significant differences between the groups in terms of demographic characteristics. Our analyses revealed that chili pepper consumption (odds ratio [OR] = 2.96, 95% confidence interval [CI]: 1.06–8.31, *P*-value = 0.039) and the duration of fissure symptoms (OR = 1.03, 95% CI: 1.00–1.05, *P*-value = 0.035) were associated with perianal fistula in patients with fissure, after adjusting for age and sex as potential covariates.

Conclusions An independent association was found between chili pepper consumption as well as the duration of fissure symptoms onset with an increased odds of perianal fistula in patients with fissures. Therefore, limiting chili consumption and early management of fissure symptoms are recommended.

Keywords Fissure in ano, Fistula, Capsicum, Rectal diseases, Case-control studies

[†]Khadije Gorgi and Zahra Ghanbarzadegan contributed similar contributions as co-first authors and Sara Shojaei-Zarghani and Ali Reza Safarpour contributed similar contributions as co-correspondence.

*Correspondence:

Ali Reza Safarpour
safarpourar@gmail.com
Sara Shojaei-Zarghani
shojaeisara@ymail.com

¹Colorectal Research Center, Shiraz University of Medical Sciences, Shiraz, Iran



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Introduction

Anal fissure is an anorectal condition characterized by a superficial ulcer or tear in the distal anal canal, which is often associated with chronic constipation or diarrhea, inflammatory bowel diseases, anal sexual intercourse, and prior anal surgery [1]. The major clinical symptoms of acute anal fissure include anal pain, spasm of the internal anal sphincter, and fresh bleeding with defecation, while chronic anal fissure (lasting >6 weeks) is characterized by hypertrophied anal papilla, exposed muscle fibers of internal anal sphincters at the base of fissure, and a skin tag at the distal end of the fissure [2]. Perianal fistula is a severe complication that may arise from a deepened anal fissure [1]. It is believed to occur due to the healing process of the distal part of the fissure, resulting in the formation of a skin bridge that facilitates the migration of fecal matter underneath it [3].

Perianal fistula is an anorectal benign disease that is characterized by an abnormal anatomical connection between the anorectal canal and the perianal area. Obstruction of the anal glands, infection, inflammatory bowel diseases, radiation, and neoplasm are among the major etiologies of perianal fistula [4]. A previous study has reported that approximately 12% of patients who underwent perianal fistula surgery had a history of anal fissure at the site of the fistula [5]. Moreover, around 82% of patients who underwent surgical management for chronic anal fissure were found to have perianal fistula [6]. It has been estimated that the progression of a fissure into a fistula may take up to two years [5]. Although some risk factors for perianal fistula development have been suggested in previous studies, including obesity, diabetes, hyperlipidemia, dermatosis, anorectal surgery, smoking and alcohol intake, excessive intake of salty and spicy/greasy foods, sedentary lifestyle, and prolonged sitting on the toilet for defecation [7], there is limited and conflicting evidence in this regard [8]. Therefore, the present case-control study was aimed to investigate the risk factors of perianal fistula development among patients with anal fissure.

Methods

This case-control study was approved by the by the Ethics Committee of Shiraz University of medical sciences, Shiraz, Iran (IR.SUMS.REC.1402.479), and all included patients provided informed consent. The case group consisted of consecutive adult patients (>18 years old) with confirmed fissure-associated fistulas diagnosis who underwent surgery at the Shahid Faghihi and Mother and Child Hospitals, Shiraz University of Medical Sciences, Iran between January 2018 and October 2023. Diagnosis of fissure-fistula was confirmed by two colorectal surgeon based on the presence of a skin tag and a superficial, mid-line low-type perianal fistula. Additionally, fissure-related

fistulas are commonly situated more caudally with a narrower external opening compared to other perianal fistulas, and the tract typically extends deep to a skin tag [3]. The control group comprised patients with chronic anal fissure who were undergoing medical treatment without any previous anorectal surgeries and consecutively visiting colorectal clinics. The mean age and sex ratio were similar between the case and control groups. The study excluded patients with comorbidities such as inflammatory bowel diseases, neurological disorders, and other perianal diseases. Additionally, individuals with a history of previous anorectal surgeries, except for fistula surgery in the case group, and those who had used steroids were also excluded from the study. Demographic, lifestyle, and clinical data were obtained through medical records or by directly contacting patients. A patient was categorized as current daily tobacco user if he/she reported daily cigarette and water-pipe usage. Chili pepper consumption and exercise were evaluated by inquiring about regular habits using single questions. The question regarding chili consumption offered four options related to the frequency of consuming foods with high red chili pepper content over the past month: "Never or only occasionally; 1–2 days per week; 3–5 days per week; daily or almost every day" [9]. Then, the participants were categorized as "not regular" (those who never consumed foods with high red chili pepper content or occasionally over the past month) or "regular" (those who consumed foods with high red chili pepper content at least 1–2 days per week over the past month) chili consumers.

Sample size was calculated by G-Power according to the body mass index >25 using a previous study [7]. Given Power=90% and considering 10% attrition, 55 subjects in the case and 55 in the control groups was investigated. The statistical analysis was carried out using SPSS software, version 25. The normal distribution of the quantitative data was evaluated using Kolmogorov-Smirnov test. The study presents qualitative, parametric qualitative, and non-parametric quantitative data as frequency (percent), mean (standard deviation [SD]), and median (interquartile range [IQR]), respectively. Differences in the qualitative and quantitative data between groups were evaluated by means of Chi-square (or Fisher's exact test) and t test (or Mann-Whitney U test if the data is non-normally distributed), respectively. Risk factors of fissure-fistula were tested using a multivariable logistic regression analysis with including potential covariates and all variables with univariable-related P -value < 0.1. The effect sizes are reported as odds ratio (OR) with 95% confidence interval. All P -values less than 0.05 were considered to indicate a significant association.

Results

Among the available records ($n=148$), the following patients were excluded: 24 subjects who did not answer the phone or declined to participate in the study (14 from the case and 10 from control group), 2 with inflammatory bowel diseases (case group), 2 individuals with multiple sclerosis or rheumatoid arthritis (control group) who were taking steroids, and one patient who had passed away (case group).

In total, 119 patients were included in the current study, comprising 54 cases and 65 controls, with a mean age of 43.19 (± 10.93). There were no significant differences between the case and control groups in terms of demographic characteristics (Table 1). The median age of the case group at fistula surgery was 40 years (IQR: 35.75–49.25), and they had undergone operations about 10 months ago (IQR: 5–24).

Upon comparing behavioral and medical features between the case and control groups (Table 2), it was observed that the proportion of patients regularly consuming chili peppers was significantly higher in the case group compared to the control group (88.9% vs. 72.3%, P -value=0.025). Additionally, the case group reported a longer duration from the onset of fissure symptoms compared to the controls, with a median of 7.5 months vs. 4 months (P -value=0.004).

Thereafter, we examined the relationship between the consumption of chili peppers and the duration of symptoms associated with fissures, while taking into account potential covariates, as outlined in Table 3. Our analysis revealed that both chili pepper consumption (OR=2.96, 95% CI: 1.06–8.31, P -value=0.039) and the duration of fissure symptoms (OR=1.03, 95% CI: 1.00–1.05, P -value=0.035) were independently associated with perianal fistula in patients with fissure.

Discussion

In the present study, we observed that patients with anal fissures who consumed red chili pepper were at an approximately three-fold increased odds of developing perianal fistula. Our findings are consistent with a prior investigation that identified spicy and greasy foods as an independent risk factor for perianal fistula [7]. Moreover, chilies and spicy foods are known to exacerbate symptoms of anal fissure. A previous randomized controlled trial (RCT) with a crossover design demonstrated that consumption of 1.5 g of dried chili powder twice daily for one week caused increased pain and anal burning compared to microcrystalline cellulose as the placebo in patients with acute anal fissures [10]. Similarly, another RCT conducted by the same author administered chili capsules to patients with chronic anal fissure and investigated postoperative symptoms such as pain, anal burning, and pruritus following closed anal sphincterotomy. The chili group reported significantly higher postoperative pain and anal burning compared to the placebo [11]. High doses of capsaicin, a major ingredient of chili pepper, have been reported to damage gastrointestinal tissues, cause colonic inflammation, and alter gut microbiota [12]. There is a positive association between perianal inflammation and fistula development [13]. However, there is conflicting evidence regarding the ulcerogenic effects of chili pepper in the gastrointestinal tract [14, 15]. Further studies are needed to better elucidate the effect and mechanism of action of chili pepper on anorectal pathologies.

Another finding from our study indicates that patients who had a prolonged duration from the onset of fissure symptoms were at an elevated odds of developing a perianal fistula. This association could be linked to the consequences of chronic non-healing or recurrent deep

Table 1 Comparison of demographic characteristics between case and control groups

Variable	Overall	Case	Control	P-value
n (%)	119	54	65	
Sex, n (%)	58 (48.7)	29 (53.7)	29 (44.6)	0.323 [†]
Male	61 (51.3)	25 (46.3)	36 (55.4)	
Female				
Ethnicity, n (%)	96 (80.7)	44 (81.5)	52 (80.0)	0.839 [†]
Fars	23 (19.3)	10 (18.5)	13 (20.0)	
Others				
Marital status, n (%)	23 (19.3)	12 (22.2)	11 (16.9)	0.239 [†]
Single	89 (74.8)	37 (68.5)	52 (80.0)	
Married	7 (5.9)	5 (9.3)	2 (3.1)	
Widowed/Divorced				
Education, n (%)	25 (21.0)	10 (18.5)	15 (23.1)	0.803 [†]
Illiterate or primary school	59 (49.6)	27 (50.0)	32 (49.2)	
Middle or high school diploma	35 (29.4)	17 (31.5)	18 (27.7)	
Academic degree				
Age at questionnaire completion (years), mean \pm SD	43.19 \pm 10.93	43.41 \pm 11.10	43.01 \pm 10.87	0.847 [*]

Abbreviations: SD: standard deviation

Between-group differences in variables were determined using independent sample t-test (*) for parametric variables and Chi-square test (†) for categorical variables

Table 2 Comparison of behavioral and medical features between case and control groups

Variable	Overall	Case	Control	P-value
Current daily tobacco use, n (%)	106 (89.1)	47 (87.0)	59 (90.8)	0.516 [†]
No	13 (10.9)	7 (13.0)	6 (9.2)	
Yes				
Alcohol intake, n (%)	109 (91.6)	49 (90.7)	60 (92.3)	0.759 [†]
No	10 (8.4)	5 (9.3)	5 (7.7)	
Yes				
History of natural vaginal delivery, n (%)	24 (47.1)	11 (47.8)	13 (46.4)	0.921 [†]
Diabetes, n (%)	9 (7.6)	4 (7.4)	5 (7.7)	1.000 [‡]
History of chronic constipation, n (%)	88 (73.9)	38 (70.4)	50 (76.9)	0.417 [†]
History of chronic diarrhea, n (%)	9 (7.6)	4 (7.4)	5 (7.7)	1.000 [‡]
Time of sitting on toilet, n (%)	22 (18.5)	11 (20.4)	11 (16.9)	0.852 [†]
< 3 min	48 (40.3)	22 (40.7)	26 (40.0)	
3–10 min	49 (41.2)	21 (38.9)	28 (43.1)	
> 10 min				
Chili pepper consumption, n (%)	24 (20.2)	6 (11.1)	18 (27.7)	0.025[†]
Not regular	95 (79.8)	48 (88.9)	47 (72.3)	
Regular				
BMI (kg/m ²), mean ± SD	27.27 ± 4.85	27.35 ± 4.35	27.19 ± 5.26	0.856 [*]
Hours of sitting a day, median (IQR)	7.00 (4.00–8.00)	6.00 (3.00–8.00)	7.00 (4.00–8.00)	0.120 [¶]
Duration of fissure symptoms onset (month), median (IQR)	6.00 (2.00–18.00)	7.50 (3.00–27.75)	4.00 (1.50–12.00)	0.004[¶]
Number of bowel movement/week, median (IQR)	7.00 (7.00–14.00)	7.00 (7.00–14.00)	7.00 (7.00–14.00)	0.732 [¶]
Number of delivery, median (IQR)	2.00 (1.00–3.00)	2.00 (1.00–2.00)	2.00 (1.00–3.00)	0.421 [¶]

Abbreviations: BMI: body mass index, IQR: interquartile range, SD: standard deviation. Between-group differences were determined using independent sample t-test for parametric variables (*), Mann Whitney U test for non-parametric parameters (¶), and Chi-square (†) or Fisher exact (‡) tests for categorical variables. Bold denotes statistical significance (P -value < 0.05)

anal fissures on the alteration of anal glands, leading to increased irritation, infection, inflammation, and eventual tissue damage in the surrounding area, culminating in fistula formation [16, 17]. Nonetheless, additional research is warranted to investigate the impact of various conservative medical treatments on fissure symptoms and the development of perianal fistulas.

There is limited evidence concerning the effects of prolonged sitting, whether total daily sitting or time spent on the toilet, on the risk of fistula development. Our study found no significant association between these factors and the development of fissure-related fistulas. This result contradicts the findings of Wang et al., who reported an 87% increased risk of perianal fistulas in Chinese individuals who had a prolonged sitting on the toilet [7]. However, the researchers did not specify the duration of sitting considered as prolonged. In Asian countries, toilets are typically in a squatting position, which is believed to facilitate faster and more complete defecation and reduce the pressure needed for bowel movements [18]. Therefore, as Wang's study was also conducted in an Asian setting, the conflicting evidence cannot be attributed to variations in the toilet type. In a separate case-control study conducted in Turkey, no independent association was found between defecation frequency or duration and perianal diseases in the multivariable model [19]. Further high-quality prospective studies with

large sample sizes are needed to better elucidate these relationships.

Our study had several limitations that should be considered during the interpretation of findings. First, the retrospective design of the current study increases the probability of recall bias. Second, the evaluation of chili pepper consumption and physical activities was conducted using a single question rather than a validated questionnaire. Third, due to the data being gathered from two hospitals affiliated with Shiraz University of Medical Sciences, the representativeness of the sample is questionable. Fourth, data regarding non-surgical treatment strategies for relieving fissure symptoms were not collected, which may have an impact on fistula development in such patients. Fifth, our sample size was small. Although the association of risk factors with perianal fistula fell within the trivial region (OR=0.8–1.2) or spanned multiple domains of interpretation, it may hold clinical significance according to the clinicians' experience.

Conclusion

According to the findings of the current study, we observed an independent association between regular chili pepper consumption and the duration of fissure symptoms onset with an increased odds of perianal fistula in patients with fissures. Consequently, a stringent management of fissure is deemed essential for the

Table 3 Risk factors of perianal fistula development among patients with anal fissure

Independent variables	Model 1				Model 2					
	B	SE	Constant	OR (95% CI)	P-value	B	SE	Constant	OR (95% CI)	P-value
Sex (Female vs. Male)	-0.365	0.370	0.000	0.69 (0.34–1.43)	0.324	-0.567	0.395	-1.389	0.58 (0.26–1.23)	0.151
Age (per 1-year increase)	0.003	0.017	-0.328	1.00 (0.97–1.04)	0.845	0.005	0.018		1.01 (0.97–1.04)	0.764
BMI (per 1-unit increase)	0.007	0.038	-0.375	1.01 (0.93–1.08)	0.855	0.001	0.040		1.00 (0.92–1.08)	0.981
Chili pepper consumption (regular vs. not regular)	1.120	0.514	-1.10	3.06 (1.12–8.39)	0.029	1.086	0.526		2.96 (1.06–8.31)	0.039
Duration of fissure symptoms (per 1-month increase)	0.024	0.011	-0.524	1.02 (1.00–1.05)	0.032	0.025	0.012		1.03 (1.00–1.05)	0.035

Abbreviations: BMI: body mass index, CI: confidence interval, OR: odds ratio. The ORs and 95% CI were determined by logistic regression. Model 1: crude, and Model 2: multivariable model. Bold denotes statistical significance (P -value < 0.05)

prevention of fistula formation. However, it is important to mention that the retrospective design of this study limits our ability to establish causal relationships. Therefore, the results should be interpreted with caution. Further prospective large-scale investigations using validated questionnaires are warranted to more comprehensively elucidate the impact of various dietary and clinical factors on the development of fistulas in fissure condition.

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Author contributions

Conceptualization and Methodology: KG, ZG, SSZ, ARS, SVH; Data curation, Formal analysis, Software: SSZ, ARS; Project administration, Validation, Supervision, and Funding acquisition: SVH; Writing – original draft: SSZ; Writing – review & editing: KG, ARS, SVH. All authors have read and approved the manuscript.

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Data availability

Data supporting the results of this study is available from the corresponding authors upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Shiraz University of medical sciences, Shiraz, Iran (Code: IR.SUMS.REC.1402.479). Informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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