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The relationship between acne vulgaris and irritable bowel syndrome: A preliminary study

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Abstract

Background: Irritable bowel syndrome (IBS) is a functional gastrointestinal disease characterized by chronic abdominal pain and changes in bowel movements without underlying organic pathology. Many skin diseases have been reported to be more common in individuals with functional bowel diseases.

Aims: In this study, we aimed to investigate a possible relationship between acne vulgaris (AV) and IBS.

Patients/Methods: This prospective controlled study included patients with AV and healthy volunteers. All the subjects were evaluated in terms of the presence of IBS. The diagnosis of IBS was made based on the ROME IV diagnostic criteria. The clinical severity of AV was calculated using the global acne grading system (GAGS).

Results: A total of 300 patients with acne vulgaris and 300 age and gender-matched healthy controls were included in the study. The majority of the patients were female (n = 175, 58.3%). The mean ages of the patients and controls were 20.22 ± 5.24 years and 20.49 ± 5.36 years, respectively. A total of 183 patients (61.0%) and 84 (28.0%) controls were diagnosed with IBS based on the Rome IV diagnostic criteria. The frequency of IBS was statistically significantly higher in the patient group than in the control group. (P = .001). There was also statistically significant relationship between the GAGS scores and IBS diagnosis (P = .001), abnormal stool form (P = .001), abdominal distention (P = .001), and feeling of incomplete evacuation (P = .001).

Conclusion: Our study showed that IBS is significantly more common in patients with AV than in healthy controls. Additionally, GAGS scores were higher in patients diagnosed with IBS. To the best of our knowledge, this is the first study focusing on the subject.

KEYWORDS

acne vulgaris, bowel, irritable bowel syndrome, skin

1 | INTRODUCTION

Irritable bowel syndrome (IBS) is a functional gastrointestinal disease characterized by chronic abdominal pain and changes in bowel movements without underlying organic pathology.[1] Its prevalence in the general population is around 10-20 percent.[2] Although IBS can be seen in all age groups, it occurs most frequently in the 30-50 age range.[3] It is suggested that the disease is caused by the interaction between multiple factors including genetic, psychological, cognitive, and environmental factors, and gastrointestinal sensory and motor functions.[2] On the other hand, the levels of mucosal and systemic proinflammatory cytokines have been shown to be increased in patients with IBS. Accordingly, it has also been suggested that inflammation may play a role in the pathogenesis of the entity.[4,5]

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit characterized by comedones, papules, pustules, and nodules, affecting almost 85% of adolescents and young adults.[6] Hypersecretion of sebum, ductal hypercornification, bacterial colonization, and the inflammatory response are the four main factors accused in the pathogenesis of the entity.[7]

The intestinal microbiota has been reported to affect acne formation by cross-interaction between the intestinal commensal bacteria and the mammalian target of rapamycin complex 1 (mTORC1) pathway. The products metabolized by the intestinal microbiota have been shown to regulate cell proliferation, lipid metabolism, and metabolic functions, in which the mTORC1 pathway also plays a role. It has also been reported that mTORC1 affects the intestinal microbiota complex by regulating the intestinal barrier.[8,9] Given the important role of mTORC1 in both the intestinal microbiome composition and acne pathogenesis,[8,9] we hypothesized that there may be a relationship between acne formation and IBS.

2 | MATERIALS AND METHODS

This prospective controlled study was approved by the Institutional Review Board (No: 2020/007), and informed consent was obtained from all the participants. Patients who were clinically diagnosed with acne vulgaris and healthy volunteers were enrolled. Patients receiving any topical or systemic therapy and with additional cutaneous or systemic diseases were excluded. Demographic features of all participants were recorded. In the patient group, the duration, severity, and family history of acne vulgaris were the evaluated parameters. The clinical severity of acne vulgaris was calculated using the global acne grading system (GAGS).[10] All the subjects were evaluated in terms of IBS. The diagnosis of IBS was made based on the ROME IV diagnostic criteria both in patients and in controls.[11] In the patient and control groups, the findings supporting the diagnosis of IBS such as the frequency of defecation, frequency of abnormal stool, forms of abnormal stool, mucous in stool, abdominal distention, and feeling of incomplete evacuation were also evaluated. Additionally, the subjects were asked to determine the stool shape and consistency according to the Bristol stool scale.[12] Patients were also asked if there was an increase in acne symptoms during IBS episodes. Subjects with "alarm findings" were excluded from the study and referred to the gastroenterologist.[13]

2.1 | Statistical analysis

Descriptive values of the data obtained were calculated as number, percentage, mean, standard deviation, median, IQR, number, and percentage. Normal distribution of the data was evaluated with the Kolmogorov-Smirnov test. The Mann-Whitney *U* test was performed for continuous variables, and the chi-squared test was used for categorical comparison of the data. The relationships between continuous variables were evaluated using correlation analysis. The differences in GAGS scores by the presence of IBS features were analyzed using Mann-Whitney *U*, Kruskal-Wallis, and ANOVA tests. Bonferroni tests were performed for multiple comparisons. The statistical significance level was set at $P < .05$. The statistical package IBM SPSS Statistics 22 was used for all analyses.

3 | RESULTS

A total of 300 patients with acne vulgaris and 300 age and gender-matched healthy controls were included in the study. The majority of the patients were female (n = 175, 58.3%). The mean ages of the patients and controls were 20.22 ± 5.24 years and 20.49 ± 5.36 years, respectively. The mean duration of acne vulgaris was 3.52 ± 2.12 years with a range of 1-12 years (Table 1). A total of 183 patients (61.0%) and 84 (28.0%) controls were diagnosed with IBS based on the Rome IV diagnostic criteria. The frequency of IBS was statistically significantly higher in the patient group than in the control group. ($P = .001$). There was no statistically significant difference between the patient and control groups in terms of the familial history of acne vulgaris and IBS (Table 2). There was also no statistically significant relationship between IBS episodes and acne development. No statistically significant difference was detected between the two groups in terms of abnormal stool frequency. The findings of abnormal stool form, abdominal distension, and feeling of incomplete evacuation were statistically significantly higher in the patient group than in the control group ($P = .001$) (Table 2). The frequency of the finding of mucus in stool was statistically significantly higher in the control group when compared with the patient group ($P = .001$). The distribution of stool patterns according to the Bristol stool scale is shown in Table 3.

There was a correlation between acne severity and stool forms. Table 4 demonstrates the correlation analysis between the acne severity by GAGS, disease duration, age, Bristol stool form, and stool frequency.

TABLE 1 Demographic features of the subjects

	Patients		Controls		
	Mean	Standard deviation	Mean	Standard deviation	*P* value
Age (year)	20.22	5.24	20.49	5.36	.215
Body mass index(kg/m^2)	23.37	4.00	23.95	3.30	**.001**
Disease duration (year)	3.52	2.12	-	-	-
Global acne grading system scores	19.88	9.03	-	-	-

Statistically significant *P* values ($P < .05$) are indicated in bold font.

TABLE 2 The analysis of clinical findings in patients and controls

	Patients		Controls		*P* value
	n	Percentage	n	Percentage	
Gender					
Males	125	41.7%	145	48.3%	.101
Females	175	58.3%	155	51.7%	
Frequency of IBS					
(−)	117	39.0%	216	72.0%	**.001**
(+)	183	61.0%	84	28.0%	
Abnormal stool frequency					
(−)	240	80.0%	252	84.0%	.202
(+)	60	21.0%	48	16.0%	
Abnormal stool form					
(−)	211	70.3%	263	87.7%	**.001**
(+)	89	29.7%	37	12.3%	
Mucus in stool					
(−)	283	94.3%	249	83.0%	**.001**
(+)	17	5.7%	51	17.0%	
Abdominal distension					
(−)	108	36.0%	219	73.0%	**.001**
(+)	192	64.0%	81	27.0%	
Feeling of incomplete evacuation					
(−)	148	49.3%	228	76.0%	**.001**
(+)	152	50.7%	72	24.0%	
Family history of acne vulgaris					
(−)	174	58.0%			
(+)	126	42.0%			
Family history of IBS					
(−)	281	93.7%	273	91.0%	.220
(+)	19	6.3%	27	9.0%	
Association of acne vulgaris and IBS episodes					
(−)	251	83.7%			
(+)	49	16.3%			
Acne severity					
Mild	151	50.3%			
Moderate	92	30.7%			
Severe	57	19.0%			

Statistically significant *P* values ($P < .05$) are indicated in bold font.
Abbreviation: IBS: irritable bowel syndrome.

Table 5 shows the statistical relationship between the mean GAGS scores and IBS-related parameters including frequency of IBS diagnosis, abnormal stool frequency, abnormal stool form, mucus in stool, abdominal distention, feeling of incomplete evacuation, and family history of IBS. There was a statistically significant relationship between the mean GAGS scores and IBS diagnosis ($P = .001$), abnormal stool form ($P = .001$), abdominal distention ($P = .001$), and feeling of incomplete evacuation ($P = .001$).

TABLE 3 Distribution of "Bristol stool form" assessment by groups

Bristol stool form scale	Patients		Controls		*P* value
	n	Percentage	n	Percentage	
1	32	10.7%	12	4.0%	**.001**
2	28	9.3%	15	5.0%	
3	64	21.3%	75	25.0%	
4	113	37.7%	150	50.0%	
5	8	2.7%	12	4.0%	
6	50	16.7%	21	7.0%	
7	5	1.7%	15	5.0%	

Statistically significant *P* values ($P < .05$) are indicated in bold font.

TABLE 4 Correlation analysis between global acne grading system (GAGS) score, age, Bristol stool form scale, stool frequency, and disease duration in the patient group

	GAGS score	Age	Bristol stool form	Stool frequency	Disease duration
GAGS score					
r	1.000				
P	.000				
Age					
r	0.034	1.000			
P	.558	.000			
Bristol stool form					
r	0.224	0.030	1.000		
P	.000	.610	.000		
Stool frequency					
r	0.044	−0.082	0.064	1.000	
P	.444	.158	.272	0.000	
Disease duration					
r	0.114	0.303	0.014	−0.089	1.000
P	.049	.000	.803	.125	.000

Abbreviation: GAGS, global acne grading system.

4 | DISCUSSION

Acne vulgaris is a multifactorial chronic inflammatory skin disease of the pilosebaceous unit, affecting 85% of adolescents.[6] Besides, genetic and hormonal factors, nutritional habits, *Propionibacterium acnes* (*P Acnes*), emotional stress, and smoking have been reported to increase acne formation.[14-19] The possible interaction between gastrointestinal factors and depression, emotional stress, and acne was first proposed by Stokes and Pillsburry.[8] The authors suggested that emotional conditions such as depression and anxiety can lead to secretion of neurotransmitters such as serotonin, norepinephrine, and acetylcholine from the intestinal enteroendocrine cells. These neurotransmitters can alter intestinal permeability and microbiota.[20-27]

TABLE 5 Analysis of the statistical relationship between the mean global acne grading system (GAGS) scores and IBS-related parameter

	GAGS scores				
Parameters	**Mean**	**Median**	**Standard deviation**	**IQR**	***P***
Gender					
Male	20.38	20.00	8.803	13	.377
Female	19.52	18.00	9.197	12	
Frequency of IBS					
(−)	13.93	13.00	6.218	8	**.001**
(+)	23.68	24.00	8.489	14	
Abnormal stool frequency					
(−)	18.65	18.00	8.728	13	**.001**
(+)	24.78	25.00	8.606	15	
Abnormal stool form					
(−)	17.38	16.00	8.043	11	**.001**
(+)	25.79	25.00	8.511	16	
Mucus in stool					
(−)	19.73	18.00	8.861	12	.398
(+)	22.35	21.00	11.527	22	
Abdominal distension					
(−)	16.06	15.00	7.277	11	**.001**
(+)	22.02	21.00	9.227	18	
Feeling of incomplete evacuation					
(−)	16.84	16.00	7.899	11	**.001**
(+)	22.84	23.00	9.102	17	
Family history of IBS					
(−)	19.59	18.00	8.769	12	.107
(+)	24.11	29.00	11.756	21	

Abbreviations: GAGS, global acne grading system; IBS, irritable bowel syndrome.

Although "the gut-brain-skin axis" hypothesis has been known for a long time, it was not well understood. However, studies on the microbiome have taken this concept a step further.[22,28] In the context of this hypothesis, the strong expression of Substance P, which is caused by the activation of the nerves containing Substance P, has been observed in both acne vulgaris and intestinal dysbiosis. Substance P triggers acne formation by secreting proinflammatory cytokines involved in acne pathogenesis.[29-32]

Irritable bowel syndrome, a chronic functional gastrointestinal disorder, is characterized by dyspeptic complaints such as recurrent abdominal pain and bloating, and changes in bowel habits such as constipation and/or diarrhea. No specific structural or biochemical markers to IBS have been described so far.[1] In this study, we used ROME IV criteria for the diagnosis of IBS. We also evaluated additional findings to support the diagnosis.[11] It has been suggested that multiple factors such as the gut-brain axis, bacterial overgrowth, psychosocial stress, low degree of intestinal inflammation, intestinal microbiota, and intestinal mucosal barrier dysfunction may play a role in the pathogenesis of IBS.[33,34]

Many skin diseases have been reported to be more common in individuals with functional bowel disease.[35,36] Ekiz et al[35] reported that patients with chronic itching of unknown origin had a higher prevalence of IBS when compared to the controls. Sholam et al reported that IBS prevalence was higher in patients with chronic urticaria than in the controls.[36]

Acne vulgaris may be associated with many gastrointestinal disorders. Hypochlorhydria allows colonic bacteria to migrate to the distal small intestine, causing bacterial overgrowth. Bacterial overgrowth causes changes in the gut microbiome, preventing the absorption of nutrients and vitamins. Malabsorption of some foods has been shown to affect the psychological state and cause acne vulgaris due to systemic oxidative stress.[37]

On the other hand, some studies provided some clues that acne vulgaris may be seen more frequently in patients with impaired intestinal permeability. In another study, 66% of 57 acne patients without additional skin disease showed higher reactivity to fecal-isolated coliform bacteria in the complement fixation test compared to controls.[38] Another study found that lipopolysaccharide endotoxins obtained from the blood of the patients with acne vulgaris showed high reactivity.[39] Liebregts et al reported that IBS patients with higher anxiety levels had higher reactivity to *Escherichia Coli* lipopolysaccharides.[40] All these studies indicate that endotoxins produced by the intestinal microbiota may trigger acne formation, and there may be a relationship between intestinal permeability and acne vulgaris.

Brain-gut-skin axis, inflammation, diets with high glycemic index, and emotional stress are the common factors playing roles in the pathogenesis of both acne vulgaris and IBS.[15-19,34] Both diseases have been shown to have increased serum levels of proinflammatory cytokines such as IL-1, IL-6, and tumor necrosis factor alpha.[5,31,41,42] These data also support the likely relationship between IBS and acne.

Our study showed that IBS is significantly more common in patients' acne vulgaris than in healthy controls. Additionally, GAGS scores were higher in patients with IBS diagnosis, abnormal stool frequency, abnormal stool form, abdominal distension, and feeling of incomplete evacuation.

To the best of our knowledge, this study, showing that there may be a strong relationship between IBS and acne vulgaris, is the first study focusing on the subject.

The relatively small number of patients is the main limitation of this study. It is obvious that more studies with larger sample size are needed to verify our findings.

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CONFLICT OF INTEREST

None.

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