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Association between Allergic diseases and irritable bowel syndrome (IBS)

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ABSTRACT

Background: Irritable Bowel Syndrome (IBS) is a functional gastrointestinal disease and the most common cause of long-term abdominal pain and bowel disorders. The association between allergic disease and IBS is limitedly understood. we aimed to investigate the frequencies of asthma, eczema and allergic rhinitis in IBS patients and as well as the relationship of these allergic diseases with IBS.

Materials and Methods: In this case-control study, we included 300 patients with IBS over 5 years of age who were referred gastrointestinal clinics of Shahid Sadoughi University of Medical Sciences, Yazd in 2021. The control group includes 300 healthy individuals without IBS. Demographic and clinical information of two groups were recorded in the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire, based on which eczema, asthma and allergic rhinitis were diagnosed. Then, the frequencies of asthma, allergic rhinitis and eczema was then compared between the two groups.

Results: The frequency of asthma was significantly higher in the IBS group (P<0.001). In addition, allergic rhinitis and eczema frequencies were significantly higher in the group with IBS compared to control group(P<0.001). It was found IBS patients were 5.37 (95%CI: 3.130-8.763) more likely to develop asthma significantly compared to healthy controls. The risk of allergic rhinitis in patients with IBS is 2.87 (95% CI: 1.900-4.084) times higher than non-IBS patients.

Conclusions: Due to the association between IBS and allergic diseases, treatment of comorbid conditions such as asthma, allergic rhinitis, and eczema may be effective in treating IBS. Our data suggest that there is a need to monitor IBS patients for the potential of developing allergic diseases, and vice versa.

Keywords: *Irritable Bowel Syndrome (IBS), asthma, allergic rhinitis, eczema*

INTRODUCTION

Irritable bowel syndrome (IBS) is the most common bowel dysfunction, but its pathophysiology is still unknown(1). Inflammation, gastrointestinal microbiota changes, bacterial overgrowth, food allergies, and environmental and genetic factors appear to be associated with the pathogenesis of IBS(2). The global prevalence of IBS is around 11%, which is more prevalent in female and young people(1, 3).

IBS is a gastrointestinal (GI) disorder determined by changes in bowel habits and abdominal pain in the absence of detectable structural abnormalities(4).A range of other gastrointestinal (GI) and non-GI signs often co-occur in patients with IBS, such as indigestion, headaches, migraine, interstitial cystitis, and fibromyalgia(5, 6). The degree of symptoms in different patients varies from tolerable to severe, and the time pattern and discomfort vary greatly in patients(7).

The association between IBS and allergies has remained controversial for several years(8). Allergic diseases such as allergic rhinitis (AR), asthma, urticaria, eczema, atopic dermatitis, and food allergies, affect approximately 20% of the population. Allergic disease can cause localized end- organ dysfunction and even systemic symptoms(9). Previous studies have shown that exposure to certain allergens may contribute to IBS-related gastrointestinal symptoms in allergic individuals(10). An increase in the number of mast cells and mediators released from active mast cells, especially histamine and tryptase , is associated with food allergies in IBS patients(8).

Allergen exposures release inflammatory mediators and induce hypersensitivity through immunoglobulin E (IgE) cross-linking on mast cells in patients with AR(11). Moreover, an increase in mast cells in the duodenum and colon was found in IBS patients(12). However, the pathophysiology of association between allergy and IBS are still unclear. And on the other hand, despite the increasing incidence of IBS in Iran, there is still a shortage of literature on IBS in the region. As regards, understanding the etiology of this disease may help cure, reduce the complications, reduce heavy costs and increase quality of life in these patients, we decided to conduct a study to assess the frequencies of asthma, eczema and allergic rhinitis in IBS patients and as well as the relationship of these allergic diseases with IBS.

METHOD AND MATERIALS

Study design and participants

This case-control study was performed on 300 patients with IBS referred to the gastrointestinal clinics of Shahid Sadoughi University of Medical Sciences, Yazd in 2021. Inclusion criteria were patients over 5 years old with IBS based on Rome IV criteria. Rome criteria are consist of: recurrent abdominal pain, on average, at least 1 day /week in the last 3 months, associated with two or more of the following criteria: related to defecation, associated with a change in frequency of stool, associated with a change in form (appearance) of stool. Criteria fulfill for the last 3 months with symptom onset at least 6 months before diagnosis. Patients with the necessary criteria were then followed up by gastroenterologist for the differential diagnosis of IBS and other related gastrointestinal diseases. Individuals under 5 years old and patients with other gastrointestinal diseases were excluded. The case group was patients with IBS, and the control group includes 300 healthy individuals without IBS. Patients and the healthy individual were matched in terms of age and sex. Information from case and control groups were recorded in the questionnaire that had been regulated according to ISAC questionnaire. Asthma, allergic rhinitis and eczema were diagnosed based on this questionnaire. Then, the frequencies of asthma, allergic rhinitis and eczema was then compared between the two groups. the study was approved by the Medical Ethical Committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran (Ethics code: IR.SSU.MEDICINE.REC.1398.166). Moreover, informed consent was obtained from all the patients, their parents, or legal guardians.

Statistical analysis

Data were analyzed using SPSS software version 22 (SPSS Inc, Chicago, IL, USA). Descriptive statistics were presented as mean ± standard deviation (SD) for quantity values and frequency (percentage) for qualitative values. Kolmogorov–Smirnov test was applied to test for the data normality. Differences were compared by using the paired sample t-test. Chi-square tests was used to investigate the correlation between qualitative variables. P-value less than 0.05 was considered significant.

RESULTS

Clinical spectrum of patients

In the present study, the frequency of asthma was significantly higher in the IBS group than the subjects without IBS ($P<0.001$). Moreover, the frequency of allergic rhinitis and eczema were higher in patients with IBS compared to the individuals without IBS ($P<0.001$) (Table 1).

Table 1. Comparison of asthma, eczema, and allergic rhinitis frequency between two groups

Groups		Patients with IBS (n=300)	individuals without IBS (n=300)	p-value
Asthma (n=110)	Yes	86 (28.6)	24 (8.0)	**<0.001***
	No	214 (71.4)	276 (92.0)	
Allergic rhinitis (n=167)	Yes	114 (38.0)	53 (17.7)	**<0.001***
	No	186 (62.0)	247 (82.3)	
Eczema (n=110)	Yes	72 (24.0)	38 (12.7)	**<0.001***
	No	228 (76.0)	262 (87.4)	

* p-value is statistically significant <0.05. n, Number.

According to the results in the Table 2, it was found IBS patients were 5.37 (95%CI: 3.130-8.763) more likely to develop asthma significantly compared to healthy controls. No significant correlation was seen between sex and having asthma. Moreover, it was indicated the villager expose to asthma 1.79 (95%CI: 1.093-2.945) more than urban dweller. Also, tobacco exposure was known as a significant factor to increase the odds of allergic diseases 2 times more (95%CI: 1.283-3.246).

Table 2. Determining the odds ratio of each of the studied variables in asthma.

		OR	p-value	CI 95%
IBS	YES	5.37	<0.001	3.130-8.763
	No REF			
Age		1	0.310	0.991-1.027
Sex	Female	1.01	0.976	0.625-1.633
	Male REF			
urbanization or rural living	Villager	1.79	<0.001	1.093-2.945
	Urban dweller REF			
contact with the tobacco.	YES	2.04	<0.001	1.283-3.246
	No REF			
contact with the animal.	YES	1.53	0.105	0.914-2.587
	No REF			

In order to evaluate the associated factors with allergic rhinitis, it was found patients with IBS had a 2.87 (95%CI: 1.900-4.084) fold greater risk of developing allergic rhinitis. Age, sex, living location, contacting with animal and tobacco were not significant factors for having allergic rhinitis. Table 3 provides more detail about these results.

Table 3. Determining the odds ratio of each of the studied variables in allergic rhinitis.

		OR	p-value	CI 95%
IBS	YES	2.87	<0.001	1.900-4.084
	No REF			
Age		1	0.98	<0.001
Sex	Female	0.89	0.588	0.607-1.327
	Male REF			
urbanization or rural living	Villager	0.96	0.872	0.627-1.487
	Urban dweller REF			
contact with the tobacco.	YES	0.91	0.668	0.600-1.388
	No REF			
contact with the animal.	YES	1.02	0.909	0.641-1.648
	No REF			

Among the studies factors which precede the eczema, patients with IBS (OR: 2.13, 95%CI: 1.36-3.33) and female sex (OR: 2.60 :1.57- 4.31) was determined as independent factor which increase the risk of eczema (Table4).

Table 4. Determining the odds ratio of each of the studied variables in eczema.

		OR	p-value	CI 95%
IBS	YES	2.13	<0.001	1.365-3.336
	No REF			
Age		1	1.02	<0.001
Sex	Female	2.60	<0.001	1.578-4.313
	Male REF			
urbanization or rural living	Villager	0.94	0.812	0.570-1.553
	Urban dweller REF			
contact with the tobacco.	YES	1.22	0.394	0.769-1.948
	No REF			
contact with the animal.	YES	0.66	0.149	0.380-1.159
	No REF			

Table 5 is shown the distribution of patients with asthma, allergic rhinitis, and eczema and IBS status in terms of exposure to tobacco, animal and living location. As it is illustrated in table 5.A a significantly relationship was found between IBS status and asthma based on contact with the animal($p<0.001$). According to the results in the Table 5.B, in non-IBS patients, the frequency of patients with asthma and allergic rhinitis were significantly higher in patients who were in contact with tobacco than others. Moreover, the distribution of asthma based on living location in IBS patients depicts a significant relation. (Table5.C)

Table 5.A. Comparison of asthma, eczema, and allergic rhinitis frequency between patients with and without IBS based on contact with the animal

Groups		Patients with IBS (n=300)			Individuals without IBS (n=300)		
contact with the animal		Yes	No	*p*-value	Yes	No	*p*-value
Asthma (n=110)	Yes	31	51	**<0.001***	9	15	0.280
	No	43	171		75	201	
Allergic rhinitis (n=167)	Yes	31	83	0.427	11	42	0.195
	No	43	143		73	174	
Eczema (n=110)	Yes	19	53	0.697	6	32	0.073
	No	55	173		78	184	

Table 5.B. Comparison of asthma, eczema, and allergic rhinitis frequency between patients with and without IBS based on contact with tobacco.

Groups		Patients with IBS (n=300)			Individuals without IBS (n=300)		
contact with the tobacco		Yes	No	*p*-value	Yes	No	*p*-value
Asthma (n=110)	Yes	31	55	0.125	15	9	**<0.001***
	No	58	156		72	204	
Allergic rhinitis (n=167)	Yes	40	74	0.108	5	48	**<0.001***
	No	49	137		82	165	
Eczema (n=110)	Yes	25	47	0.281	12	26	0.708
	No	64	164		75	187	

Table 5.C. Comparison of asthma, eczema, and allergic rhinitis frequency between patients with and without IBS based on urbanization or rural living.

Groups		Patients with IBS (n=300)			Patients without IBS (n=300)		
urbanization or rural living		urbanization	rural living	*p*-value	urbanization	rural living	*p*-value
Asthma (n=110)	Yes	43	43	**<0.001***	12	12	0.085
	No	146	68		186	90	
Allergic rhinitis (n=167)	Yes	74	40	0.591	36	17	0.744
	No	115	71		162	85	
Eczema (n=110)	Yes	45	27	0.920	26	12	0.736
	No	144	84		172	90	

** p-value is statistically significant <0.05*

DISCUSSION

Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder with a range of symptoms that noticeably affect quality of life for patients(14). Current study was aimed to assess the frequencies of asthma, eczema and allergic rhinitis in IBS patients and as well as the relationship of these allergic diseases with IBS. In recent decades, several studies have examined the association between asthma and IBS(15). The study of Shen et al. showed the incidence of asthma was 1.76 times higher in the IBS group than the control group with an aHR (adjusted hazard ratio) of 1.54 (95% CI = 1.44−1.64)(16). The findings of this study were similar to our study. Based on our findings, the frequency of asthma was significantly higher in the IBS group (n=86, 28.0%) than control group (n=24, 8.0%)(P<0.001).

In a case-control study, Yazar et al. showed that the frequency of asthma in IBS patients was much higher than in healthy subjects (15.8 vs. 1.45%) according to medical history, clinical features, and pulmonary function test results(17). In another study using the medical records of 30,000 patients, Jones et al. founded that IBS patients had a higher frequency of asthma than healthy subjects (15.0 vs. 11.0%)(12).

These findings are consistent with the results of the current study: IBS patients are at higher risk for asthma. The mechanisms of the two-way

association between asthma and IBS or the concomitant causes of these two diseases are largely unknown. Atopy may play a key role in communication(16).

Although our study showed a significant association between asthma and IBS in patients, previous studies around the world have shown different results. Investigations from South Korea(18) and Italy(19) have demonstrated no association between IBS and asthma.

Contrary to our study, the study of Siddiqui et al. showed the frequency of asthma in the IBS group was 17.14% as compared to 20%in control group. According chi-square test, the OR for frequency of asthma in IBS as 0.828 with 95% CI between 0.320 and 2.121 (P=0.664) which was non-significant(4).

The association between IBS and asthma may have a regional variation. Numerous studies from Europe have reported that the presence of regional, genetic, environmental and socio-economic factors may lead to the presence of this association in that region(4).

Allergic rhinitis frequency was significantly higher in the group with IBS than in the control group [(n=114, 38.0%) vs. (n=53, 17.0%), p<0.001]. Similar to our study, Lauriello et al. found a significant association between allergic rhinitis and IBS(20). Also, Tan et al. performed a population-based case-control study and showed the highest OR (i.e., 1.78) for IBS in patients with AR (95% CI 1.69–1.87) among all antecedent allergies in children, followed by an OR of 1.56 (95% CI 1.40–1.73) in children with urticaria(8). Contrary to our findings, Nybacka et al. showed that presence of atopic disease was reported in 55% of patients with IBS compared to 40% of controls (P =0.07)(21).

In a study by Ronmark et al., Which investigated on 1172 patients with the risk factors for asthma, allergic rhinitis and eczema, concluded that the frequencies of these three diseases decreases with age, but by examining the odds ratio for the regression model, age was not a risk factor for any of these diseases(22), but in our study, female gender was a risk factor for asthma.

According to our study, there was no significant relationship between age, smoking, urban/rural life, and contact with animals with allergic rhinitis. While, Ronmark et al. concluded that the frequency of rhinitis decreases with age, but by examining the odds ratio in a regression model, age and female gender are not a risk factor for rhinitis. Also, urban / rural life was not associated with the frequency of allergic rhinitis, and tobacco exposure was not a risk factor for the disease(22). In the study of Ziyab et al., There was no significant correlation between age, sex and exposure to tobacco with allergic rhinitis, but contact with animals increased the risk of rhinitis(23).

CONCLUSION

According to our study, a significant association was observed between asthma, allergic rhinitis and eczema with IBS. Due to the fact that the treatment of IBS is mostly a change in diet and diet, studies can be done to use the treatment of allergic diseases on the process of IBS. There are several limitations to our study. The first limitation of this study was the relatively small number in the control and case groups, so we don't have enough power to detect real differences in the frequency of allergic diseases between patients with IBS compared to our control group. Second, relevant clinical variables, such as pulmonary function tests, serum laboratory data, or imaging results, were not available to confirm the diagnosis. The findings of our study, and in similar previous reports, indicate the need for larger population-based multicenter studies to link IBS to allergic diseases. If there is a real link between IBS and allergic diseases, this requires a multidisciplinary health care team approach to providing good quality care to patients with IBS.

CONFLICT OF INTERESTS

The authors report no conflict of interests.

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