Post-Infectious Irritable Bowel Syndrome after an Epidemic of Gastroenteritis in South of Iran

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Abstract

Background:
Irritable bowel syndrome (IBS) is a chronic disabling condition without a well-defined etiology. Infectious gastroenteritis (IGE) has been linked to this syndrome. There are few data from Iran on this association.

Methods:
In August 2018, an epidemic of IGE caused by *Escherichia coli* occurred in a village in the west of Shiraz in southern Iran. One year after this epidemic, the occurrence of IBS was surveyed in those who suffered from IGE based on Rome IV criteria in that village.

Results:
Of 179 patients included in the present study, 17 patients (9.5%) had post-infectious (PI)-IBS. There was no difference in age, sex, antibiotic use, hematochezia, duration of infectious diarrhea, fever, and weight loss at the time of IGE between those with and without PI-IBS.

Conclusion:
PI-IBS is common after IGE, but no risk factor for its development was found in this study.

Keywords:
Irritable bowel syndrome, Enteritis, Risk factors, Epidemiologic study characteristics

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Introduction

Irritable bowel syndrome (IBS) is a functional gastrointestinal (GI) disorder characterized by chronic abdominal pain and change in bowel habits with unknown etiology.[1] It is estimated that the incidence of IBS is 38.5 per 10 000 person-years,[2] and the prevalence has been reported to be 10-17% in the general population.[3-5]

This disabling disease imposes a great economic burden,[6] can result in absenteeism from school or work, and could impair the patients' quality of life.[7]

The most recent diagnostic criteria for this condition is Rome IV criteria, according to which IBS is classified into constipation-dominant, diarrhea-dominant, mixed, or unsubtyped IBS (based on the stool consistency).[8,9]

IBS is considered a multifactorial disease, and several risk factors have been linked to it, which include patient's age, sex, genetics, diet, psychosocial status, altered microbiota, subclinical inflammation, and hypersensitivity of neural network.[10,11] Nevertheless, the pathogenesis of IBS seems to be complex and still not well understood.

One of the substantial factors recognized as a risk factor for IBS is infectious gastroenteritis (IGE), which can result in microbial imbalance and may impair the mucosal functions, sensitize the nerves, and activate the immune system, resulting in a change in the expression and release of local inflammatory mediators and cytokines.[12] Most post-infectious IBS (PI-IBS) cases are reported after bacterial infections with *Campylobacter jejuni*, *Salmonella enterica*, *Shigella sonnei*, *Clostridium difficile*, and *Escherichia coli* rather than viral and protozoal infections.[13]

Several risk factors have been suggested to increase the patients' susceptibility to PI-IBS, which include genetic factors, altered intestinal microbiota, female sex, younger age, severity and duration of the initial IGE, and psychological factors.[14] Yet, conflicting results have been reported for the role of body mass index (BMI) and other demographics in the pathogenesis of PI-IBS.[2] There are few, if any, prospective studies of PI-IBS from Iran. This study was designed to determine the incidence and characteristics of this condition after an outbreak of IGE in the south of Iran.

Materials and Methods

Study Design

In August 2018 an epidemic of IGE occurred in a rural community in Sepidan county (Figure 1) because of the contamination of water sources with sewage. The causative organism was found to be enteroinvasive *E. coli*. Those who developed gastroenteritis in this epidemic were followed up after 1 year for the presence of new-onset IBS based on Rome IV criteria and the clinical diagnosis of the gastroenterologist. The patients with known malabsorptive diseases before the epidemic, including those with celiac disease, prior abdominal surgery, gastrointestinal malignancy, and inflammatory bowel disease, were not included in the study. Excluded also were those with IBS before the epidemic.

The demographic data, as well as diet, characteristics of IGE at the beginning, and use of antibiotics were recorded. All the participants were visited after 1 year in 2019, and a medical interview was done with an emphasis on Rome IV criteria for PI-IBS.

Figure 1. Map of Sepidan county in Fars province.

Statistical Analysis

The descriptive results of the categorical variables were presented by frequency (percentage) and compared between the two study groups using the chi-square test. The only quantitative variable was patients' age, described by mean±standard deviation (SD). The results of the one-sample Kolmogorov-Smirnov test showed that the patients' age did not have normal distribution; thus, a comparison between the groups was performed using Mann-Whitney U test. For the statistical analysis, the statistical software IBM SPSS Statistics for Windows version 21.0 (IBM Corp. 2012. Armonk, NY: IBM Corp) was used. P values <0.05 were considered statistically significant.

Results

Of 179 patients included in the present study, 17 patients (9.5%) had PI-IBS 1 year after IGE. The median (IQR) age of patients in PI-IBS group was 31(15-37) years, and in the IGE group was 30 (18-38) years ($P=0.64$). More than half (58.8% in PI-IBS group and 50.6% in those without IBS) were women ($P=0.62$). More than half were married in both groups ($P=0.52$). Considering the enteritis-related characteristics, the frequency of abdominal pain, antibiotic use, hematochezia, diarrhea for more than 7 days, fever, and weight loss were not different between two groups ($P>0.05$; Table 1).

Discussion

The present study showed a prevalence of less than 10% for PI-IBS in the included patients (with IGE),

Table 1. Univariate comparative analysis between the two groups of participants with enteritis after 1 year

	Variables		Enteritis with post-infectious IBS (17, 9.5%)	Enteritis without post-infectious IBS (162, 90.5%)	*P* value
Host-related factors	Age (y), mean ± SD		26.94 ± 11.10	29.64 ± 13.15	0.64[a]
	Gender, No. (%)	Male	7 (41.2)	80 (49.4)	0.62[b]
		Female	10 (58.8)	82 (50.6)	
	Marital status, No. (%)	Single	8 (47.1)	76 (46.9)	0.52[b]
		Married	9 (52.9)	86 (54.1)	
Enteritis-related factors (during enteritis)	Abdominal pain, No. (%)	Yes	13 (76.5)	103 (63.6)	0.29[b]
		No	4 (23.5)	59 (36.4)	
	Antibiotics use, No. (%)	Yes	9 (52.9)	50 (30.9)	0.20[b]
		No	8 (47.1)	112 (69.1)	
	Bloody diarrhea, No. (%)	Yes	1 (5.9)	4 (2.5)	0.42[b]
		No	16 (94.1)	158 (97.5)	
	Diarrhea > 7 days, No. (%)	Yes	1 (5.9)	11 (6.8)	0.88[b]
		No	16 (94.1)	151 (93.2)	
	Fever, No. (%)	Yes	6 (35.5)	27 (16.7)	0.06[b]
		No	11 (64.7)	135 (83.3)	
	Weight loss, No. (%)	Yes	1 (5.9)	19 (11.7)	0.46[b]
		No	16 (94.1)	143 (88.3)	

IBS, Irritable bowel syndrome.
[a] The result of Mann-Whitney U test, [b] The results of chi-square test.

which is within the range of previous review studies (4-36%).[15,16] The review study by Klem and colleagues also reported a pooled prevalence of 11.5%,[17] which is close to that reported in the present study, although the sample size of the present study was limited. Furthermore, there are several factors that can result in different PI-IBS rates reported among different studies, such as the definition criteria used for the diagnosis of IBS. As stated above, we used the most recent definition, Rome IV, while studies published before 2016 had used Rome III or older versions.[8] The prevalence of IGE in the study population and the occurrence of IGE outbreaks can also influence the incidence rates of PI-IBS.[18] The cause of IGE can also play a role in the incidence of PI-IBS; for instance, PI-IBS has been reported in 5.4% of patients after travelers' diarrhea.[19]Also, about half of patients with IGE caused by protozoa and parasites developed PI-IBS, while it was observed in less than 14% of cases with bacterial IGE.[17] However, we considered patients from one single epidemics of acute IGE in the present study. Another factor that contributes to the different incidence rates reported is the interval between IGE and IBS diagnosis, which differs among studies.[14] Larger epidemiological studies are required for reporting reliable incidence and prevalence rates.

A comparison of different variables in the present study between the patients with and without IBS was performed to identify the possible risk factors of PI-IBS in the study population. Studying the demographic variables showed that neither female sex nor patients' age were different between the study groups. This is while most review studies report female sex and younger age as risk factors of PI-IBS.[14,17] In the study by Lacob and colleagues, comparing patients with PI-IBS with a control group showed that women had a 4.4-fold increased odds of developing PI-IBS (versus men).[20] This can be because of the increased level of psychological disorders in women, including depression, anxiety, and stress, which have been identified as important factors predisposing the patient to PI-IBS.[21] Younger age has also been introduced as a predisposing factor for PI-IBS, and age > 50-60 years old has been suggested to protect against PI-IBS, possibly because of the poorer activation of the immune system.[22] However, in our study, we did not

observe such an effect on patients' sex or age.

Besides the demographic characteristics, we examined the difference in the clinical characteristics between the two study groups, and the results showed that the presence of symptoms, such as abdominal pain, hematochezia, diarrhea for more than a week, fever, and unintentional weight loss was not different between the two study groups. Abdominal pain is one of the main and most disturbing symptoms of IBS, as well as PI-IBS, supposed to be related to the patient's bloating, diarrhea, and constipation in the patients. The focus of therapy is also centered on patients' abdominal pain and response to treatment is evaluated by measuring this symptom.[23,24] However, the presence or absence of pain or other clinical symptoms cannot differentiate PI-IBS.[25] The similar frequency of abdominal pain in the two groups of the present study also confirmed these results. Unintentional weight loss and hematochezia are considered the two alarming signs of IBS, which call for the use of more accurate diagnostic tools, such as colonoscopy, to rule out important differential diagnoses.[16] The results of the present study showed that the patients of the two study groups did not differ in the frequency of weight loss or hematochezia, which then again confirms that the clinical symptoms cannot be used for differentiating between PI-IBS and IBS not related to acute gastroenteritis (AGE).

Fever is another alarming sign of IBS, considered one of the risk factors of PI-IBS, and included in the diagnostic criteria used for confirmation of AGE in PI-IBS.[22,26] However, the results of the present study did not show any difference in the frequency of fever between the two study groups. In addition, we found no difference in the frequency of antibiotic use between the two study groups. Antibiotics are considered a two-blade sword in IBS,[27] the inappropriate use of antibiotics can result in changes in the intestinal microbiota and flora that can predispose the patient to PI-IBS,[17] while antibiotics are suggested as an effective treatment for PI-IBS, especially in cases with the constipation-dominant type.[21,28] It has been suggested that antibiotics can control the small intestine bacterial overgrowth in patients with IBS and reduce the inflammation of the intestinal mucosa.[29] However, the exact mechanism of action for the effect of antibiotics in PI-IBS is still not well understood, and the results of the studies are controversial[30]; therefore, more studies are required in this regard.[16]

Some limitations should be noted. First, the small sample size and non-randomized selection of patients from one medical center in one city increase the chance of bias in the results and the effect of confounders. Second, to diagnose the IBS, a colonoscopy was not performed because of the patients' disagreement with the colonoscopy. Third, all the information in this study was extracted from the hospital records that were recorded at the time of gastroenteritis, and there may be a lack of information about some parts of the data. Therefore, great precautions should be taken for the generalizability of the results to other populations. In addition, the retrospective nature of the study limited the suggestion of a causal relationship between the variables as well as the evaluation of other factors that could also contribute as a risk factor of PI-IBS, such as the type of infection, which could not be evaluated in this study.

Conclusion

The results of the present study did not show any difference in the patients' characteristics and enteritis-related symptoms between PI-IBS patients and those with IGE alone. Further prospective studies with a larger sample size are required for definite conclusions about the factors contributing to PI-IBS.

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Ethical Approval

The protocol of the study was approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.MED.REC.1400.419). All participants gave informed consent before enrolling in the study.

Conflict of Interest

The authors declare no conflict of interest related to this work.

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