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# Post-infectious irritable bowel syndrome in a paediatric population: first data in a Middle Eastern country

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## Abstract

**Background** Acute gastroenteritis (AGE) is the second most common cause of paediatric hospitalizations and mortality worldwide. The type of etiological agent determines its clinical severity. Interestingly, AGE has been shown as a risk factor for the development of post-infection irritable bowel syndrome (PI-IBS). In this study, we aimed to correlate the clinical severity of AGE for different infectious etiologies with the occurrence of PI-IBS in North Lebanese children and adolescents.

**Methods** A total of 219 patients admitted with gastrointestinal complaints, aged between four and 15 years, were enrolled in this study. For each patient, a stool sample was obtained for microbiological analysis. Data on demographic and socioeconomic characteristics, and clinical history were collected. AGE severity was evaluated using the Vesikari Clinical Severity Scoring System. The patients were then followed to assess the development of PI-IBS, using the Bristol stool form scale and the Rome IV diagnostic criteria.

**Results** Viral pathogens were the predominant etiological agents of AGE (26.9%), followed by parasites (8.2%), and *Salmonella* spp. (4.6%). Of all the pathogens identified in this study, rotavirus was the predominant infectious agent (25.1%) associated with severe AGE. Children with parasitic or bacterial AGE had significantly higher C-reactive protein (CRP) average levels ( $p=0.009$ ). Moreover, 29 patients (13.24%) met the Rome IV criteria for PI-IBS, with mixed bowel habits (IBS-M) (48.3%) as the most frequent subtype.

**Conclusion** This study provided novel preliminary data on the development of PI-IBS in Lebanese children and adolescents. Further studies are needed to explore the pathogenesis of PI-IBS and possible prevention strategies.

**Clinical trial number** Not applicable.

**Keywords** Acute gastroenteritis, Post-infectious irritable bowel syndrome, Children, Adolescents, Stool, Rome IV criteria

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## Introduction

The prevalence of acute gastroenteritis (AGE) increases significantly in low-to-middle-income countries (LMIC) [1] such as South Asia (38%) and Africa (46%) [1]. In the Middle East and North Africa (MENA) region, AGE causes over 4 million episodes and almost 34,000 deaths each year [2]. Travel history to such endemic areas should be considered within diagnostic testing to identify the causative pathogen [3]. AGE can result in microbial dysbiosis, impair barrier functions and evoke inflammatory responses, leading to an increased expression and release of proinflammatory cytokines [4]. Thus, AGE is associated, in a subset of cases (4–36%), with subsequent irritable bowel syndrome (IBS) in children after the clearance of the culprit pathogen [5]. This phenomenon is referred to as post-infectious IBS (PI-IBS) in individuals who have not been diagnosed with IBS previously. Research has shown that PI-IBS most often develops following AGE caused by invasive pathogens (bacteria or parasites) rather than a viral infection [5]. The prevalence rate of PI-IBS demonstrates a wide variation in different populations. Estimates have ranged between 3.7% and 85.5%, with a pooled prevalence of 11.5% [6]. Moreover, previous studies have reported that male sex, younger age and severity of AGE are associated with PI-IBS development [5, 7].

Criteria for PI-IBS diagnosis have been recommended by the Rome Foundation Working Group, based on Rome IV criteria, fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis (Box 1) [8]. Based on the predominant stool pattern graded on the Bristol stool form scale, this condition is categorized into four subtypes: diarrhoea-predominant IBS (IBS-D), constipation-predominant IBS (IBS-C), mixed bowel habits (IBS-M) and unclassified (IBS-U) [9]. The pathogenesis of PI-IBS depends on the infectious agent, host and host–pathogen interactions [7]. Various infectious

### Box 1 Diagnostic Criteria for Post-Infectious Irritable Bowel Syndrome (adopted from [8])

1. Recurrent abdominal pain, on average, at least 1 day per week in the last 3 months, with symptom onset at least 6 months before diagnosis, associated with two of the following:

- a) defecation
- b) a change in frequency of stool
- c) a change in form (appearance) of stool

2. Symptom development immediately after resolution of acute infectious gastroenteritis

3. Infectious gastroenteritis defined by positive stool culture in a symptomatic individual or presence of two of the following acute symptoms (when stool culture not available):

- a) fever
- b) vomiting
- c) diarrhoea

4. Should not meet criteria for IBS before onset of acute illness

diseases have been associated with the development of PI-IBS; however, in contrast to other pathogens, parasitic gastroenteritis exhibits the greatest risk of developing PI-IBS [10]. Increased mucosal damage and inflammation have been found to be more common in bacterial infections than in viral gastroenteritis. These findings prove that patients with bacterial gastroenteritis are more likely to develop PI-IBS than those with a viral infection [5]. Previous studies have described the relationship between PI-IBS and numerous infectious agents, including norovirus, rotavirus, *E. coli*, *Salmonella*, *Shigella*, *Campylobacter*, *Clostridium difficile* and *Giardia* [10].

Data on PI-IBS in the Middle East region is scarce. Thus, the primary objective of this study was to investigate new-onset PI-IBS development among laboratory-confirmed cases of AGE in a paediatric population, and to evaluate the association between patient characteristics and PI-IBS development.

## Materials and methods

### Study design and data collection

This prospective study included children and adolescents, aged between four and 15 years old, admitted to three hospitals in North Lebanon between October 2023 and June 2024. Paediatric patients ( $n=219$ ) residing in the North governorate and presenting with gastrointestinal (GI) disturbances were included in the study. Children and adolescents diagnosed with non-infectious diarrhoea, congenital malformations, inflammatory bowel disease (IBD), previous history of IBS or history of immunodeficiency were excluded.

A stool sample was collected from each patient. Data including demographic and socioeconomic characteristics, hospitalization history and clinical manifestations was obtained through face-to-face interviews using a semi-structured questionnaire. The clinical severity of gastroenteritis was evaluated on initial admission by the Vesikari Clinical Severity Scoring System as follows: severe (above 10 points), moderate (between 7 and 10), and mild (less than 7 points) [11]. Patients were followed for six months post-AGE to complete the Rome IV questionnaire for diagnosing PI-IBS. Questions were asked to rule out IBD, microscopic colitis and celiac disease.

### Specimen collection and laboratory investigations

A fresh stool sample was collected from each patient and transported to the laboratory for parasitological analysis using direct saline wet-mount microscopy [12]. Moreover, modified acid-fast staining was used to detect oocysts of the coccidian parasitic species. The presence of rotavirus and adenovirus was investigated using the Rotavirus and Adenovirus Combo Rapid Test Cassette (MedNet GmbH, Germany), according to the manufacturer's instructions. For bacterial detection, stool cultures

were performed upon the physician's request. Stool specimens were inoculated on eosin methylene blue agar and in selenite enrichment broth for 24 h at 37°C. The medium was then subcultured on *Salmonella-Shigella* agar at 37°C for 48 h. Suspected colonies were detected based on their characteristic appearance on agar plates, and these were further tested by the API20E identification system (BioMérieux, Paris, France).

Laboratory results for white blood cell (WBC) counts and C-reactive protein (CRP) concentrations were retrieved from the medical records.

### Statistical analysis

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) program (version 21.0). Descriptive statistics (means and standard deviations (SD)) were presented for continuous variables. Frequencies and percentages were reported for categorical variables. Discrepancies in demographic characteristics and clinical manifestations among the studied groups were determined using a bivariate analysis (Chi-squared test) for categorical variables. For continuous variables, an independent t-test was performed.

Differences in patients' characteristics between IBS and non-IBS groups were compared using the Chi-squared test. Simple binary logistic regression was performed to evaluate the relationship between patient characteristics and the development of PI-IBS. A p-value of less than 0.05 is considered to be statistically significant.

## Results

### Distribution of infectious agents in the enrolled patients

The pathogens were identified in less than half of the children and adolescents. They were distributed as follows: viruses (59, 26.9%), parasites (18, 8.2%) and *Salmonella*

spp. (10, 4.6%). Mixed infections were identified in 4.6% of the patients. However, 55.7% of the cases were not identified. Rotavirus and adenovirus were found in 25.1% and 1.8% of the mono-infections, respectively. Regarding the parasitic species, *E. histolytica* was detected in 4.7% of the patients, whereas *Giardia lamblia* was observed in 3.5% of the cases.

Table 1 shows the association between patient characteristics and each of the causative agents. No significant difference in the distribution of pathogens was observed with regard to sex. In terms of clinical manifestations, high-grade fever was significantly more common in patients infected with *Salmonella* spp. ( $p < 0.002$ ); however, vomiting was recorded less often ( $p < 0.001$ ). Nausea was common in children and adolescents diagnosed with adenovirus, parasitic or mixed infections ( $p = 0.007$ ). Age, crowding index, CRP and WBC levels were not associated with the type of infectious agent. Significant differences were also observed in the average Vesikari score, with the highest scores recorded in participants with rotavirus or mixed pathogens ( $p < 0.001$ ).

### Distribution of PI-IBS subtypes

Among the confirmed cases of IBS (29; 13.24%), 48.3% exhibited symptoms consistent with IBS-M ( $n = 14$ ), 37.9% with IBS-D ( $n = 11$ ) and 13.8% with IBS-C ( $n = 4$ ). The demographic and clinical variables were then evaluated according to PI-IBS (Table 2). Female patients and those diagnosed with parasitic—especially *G. lamblia*—or mixed infections were significantly more likely to develop IBS ( $p = 0.026$  and  $p < 0.001$ , respectively). Furthermore, nausea was significantly more common among children with PI-IBS ( $p = 0.001$ ).

**Table 1** Demographic characteristics and clinical manifestations among the study groups ( $n = 219$ )

	Rotavirus	Adenovirus	Ent-amoeba histolytica	Giardia lamblia	Salmonella spp.	Mixed	Unidentified	Total	p-value
<b>Sex</b>									
Male	30 (54.5)	1 (25.0)	5 (45.5)	4 (57.1)	4 (40.0)	4 (40.0)	62 (50.8)	110 (50.2)	0.884*
Female	25 (45.5)	3 (75.0)	6 (54.5)	3 (42.9)	6 (60.0)	6 (60.0)	60 (49.2)	109 (49.8)	
<b>Clinical manifestations</b>									
Fever	12 (21.8)	0 (0.0)	0 (0.0)	0 (0.0)	7 (70.0)	1 (10.0)	38 (31.1)	58 (26.5)	<0.002*
Diarrhoea	55 (100.0)	4 (100.0)	11 (100.0)	7 (100.0)	10 (100.0)	10 (100.0)	118 (96.7)	215 (98.0%)	0.708*
Vomiting	43 (100.0)	4 (100.0)	8 (72.7)	6 (85.7)	1 (10.0)	7 (70.0)	46 (37.7)	115 (52.5%)	<0.001*
Nausea	8 (14.5)	1 (25.0)	5 (45.5)	1 (14.3)	1 (10.0)	3 (30.0)	9 (7.4)	28 (12.8)	0.007*
Abdominal pain	12 (21.8)	2 (50.0)	1 (9.1)	2 (28.6)	2 (20.0)	2 (20.0)	11 (9.0)	32 (14.6)	0.039*
<b>Age</b>	5.1 ± 1.7	4.0 ± 0.0	5.8 ± 1.5	6.0 ± 2.6	6.5 ± 2.6	6.4 ± 2.5	5.8 ± 2.6	5.6 ± 2.4	0.171
<b>Crowding index</b>	2.5 ± 1.6	2.5 ± 1.1	2.5 ± 1.4	3.5 ± 2.5	2.2 ± 0.7	2.8 ± 1.2	2.6 ± 1.3	2.6 ± 1.4	0.126
<b>CRP</b>	15.3 ± 18.6	9.2 ± 8.9	74.1 ± 93.5	16.2 ± 12.7	49.0 ± 47.8	19.3 ± 17.2	24.1 ± 37.0	24.8 ± 39.2	0.690
<b>WBC</b>	13.4 ± 5.9	10.0 ± 5.3	13.2 ± 6.5	14.4 ± 4.9	17.6 ± 9.4	12.1 ± 5.7	13.5 ± 8.6	13.6 ± 7.7	0.180
<b>Vesikari score</b>	12.1 ± 2.3	8.5 ± 3.3	8.6 ± 2.9	11.6 ± 3.4	8.8 ± 3.4	13.1 ± 2.6	10.0 ± 4.4	10.5 ± 3.9	<0.001

\* Cells have expected count less than 5—used Fisher's test instead of Pearson Chi-Square

**Table 2** Demographic and clinical characteristics of patients enrolled in this study ( $n = 219$ )

	No-IBS	IBS	p-value
<b>Type of pathogen</b>			
Rotavirus	55 (28.9)	0 (0.0)	<0.001*
Adenovirus	3 (1.6)	1 (3.4)	
<i>Entamoeba histolytica</i>	7 (3.7)	4 (13.8)	
<i>Giardia lamblia</i>	3 (1.6)	4 (13.8)	
<i>Salmonella</i> spp.	8 (4.2)	2 (6.9)	
Mixed	3 (1.6)	7 (24.1)	
Unidentified	111 (58.4)	11 (37.9)	
Total	190 (100.0)	29 (100.0)	
<b>Age</b>			
< 10 years	172 (90.5)	26 (89.7)	1.000*
10 years and more	18 (9.5)	3 (10.3)	
<b>Sex</b>			
Male	101 (53.2)	9 (31.0)	0.026
Female	89 (46.8)	20 (69.0)	
<b>Vesikari score</b>			
Mild	31 (16.3)	5 (17.2)	0.860*
Moderate	62 (32.6)	8 (27.6)	
Severe	97 (51.1)	16 (55.2)	
<b>Clinical manifestations</b>			
Fever	50 (26.3)	8 (27.6)	0.885
Diarrhea	187 (98.4)	28 (96.6)	0.436*
Vomiting	95 (50.0)	20 (69.0)	0.057
Nausea	18 (9.5)	10 (34.5)	0.001*
Abdominal pain	30 (15.8)	2 (6.9)	0.164*

\* Cells have expected count less than 5—used Fisher's test instead of Pearson Chi-Square

## Discussion

Infectious agents were identified in 44.3% of children and adolescents; among them, 4.6% were mixed pathogens. The concurrent infections percentage reported in this study is lower than the findings of a previous study conducted in Beirut (11.45%) and higher than those shown in an Italian study (2.3%) [13, 14]. Among the identified etiologic agents, rotavirus was reported predominantly (25.1%) in patients younger than ten years old. This percentage is higher than previously reported findings in Lebanon [15, 16]. In contrast to the other pathogens, rotavirus was significantly associated with severe AGE. These findings, which are expected in hospital settings, are in line with other studies conducted in the Middle East [17, 18].

Furthermore, 8.2% of the patients were infected with protozoan intestinal parasites, including *E. histolytica*, the second etiological agent of AGE in our study. In comparison to our results, higher frequencies of *E. histolytica* infection were previously reported among children residing in Beirut and in many neighbouring countries, including Libya, Yemen, Saudi Arabia and Iraq [14, 17, 19–22]. These discrepancies could be attributed to variations in social, economic and environmental characteristics, as

well as geographical locations. Moreover, these patients showed the highest CRP level. This finding was supported by previous studies that have reported a correlation between high levels of CRP and increased uptake of some parasites into macrophages [23, 24].

Our findings showed that 55.7% of the cases were reported with unidentified pathogens. The underestimation of some enteric organisms, by both paediatricians and clinical microbiology laboratories in the country, can explain this notable percentage. These pathogens (e.g. *Campylobacter* spp., *Clostridium difficile*, *Cryptosporidium* spp., norovirus and sapovirus) are excluded from the routine screening of diarrhoeal cases, resulting in mistreatment and inappropriate antimicrobial prescribing. Thus, advanced and powerful diagnostic tools in test panels are crucial for the accurate microbial identification of neglected pathogens.

The overall frequency of PI-IBS was 13.24%. This finding is lower than the prevalence (30%) reported in an American study [25] but within the range of previous reports [5]. Many factors can explain these discrepancies. First, Rome IV criteria were used for the diagnosis of IBS in this study, whereas older versions were used in studies conducted before 2016 [26]. Other factors may also play a role in the rate differences, including the type of causative agent and the time interval between AGE and IBS diagnosis among studies [27]. The predominant PI-IBS subtype in this study was IBS-M (48.3%). This finding is consistent with other studies that reported IBS-M as the most common phenotype; however, it is inconsistent with another study that documented IBS-D as the predominant type [28]. Our findings showed that female sex was significantly associated with an increased risk of developing PI-IBS. Several other studies have also demonstrated the contribution of the female sex to higher odds of developing PI-IBS [28]. Moreover, a recent Romanian study showed a higher prevalence of PI-IBS among female subjects [29]. With regard to the clinical manifestations, a higher percentage of PI-IBS patients reported nausea. This finding is consistent with a Dutch prospective multicentre study that reported nausea as a predictor for PI-IBS development following traveller's diarrhoea [30]. Furthermore, our findings revealed that patients with parasitic infections or co-infections and those with severe AGE were more prone to PI-IBS. These findings are consistent with other studies that demonstrated previous infection with enteric parasites and severity of AGE as risk factors for PI-IBS [6, 31–33]. However, the small number of parasitic infection cases is insufficient to draw a valuable conclusion. Several studies conducted in Norway and Spain have highlighted this association, with a high frequency [33–35]; however, the current research shows varied findings, where heterogeneity in the time interval between first exposure to

*Giardia* and PI-IBS development among studies makes for challenging comparisons.

This study has some limitations. The microbiological tests were limited to routine investigations and the stool cultures were only performed upon medical request. Therefore, some diarrhoeal etiologies not being routinely tested in Lebanese clinical laboratories highlights the urgent need to diagnose microbial agents using accurate molecular techniques. Moreover, future studies should focus on the specific impact of a single pathogen in order to attain precise results. Nevertheless, this study can aid in evaluating patients at greater risk for PI-IBS, who may need further examination in longer follow-up periods.

## Conclusions

Our findings shed light on the occurrence of PI-IBS in Lebanese children and adolescents, with most patients exhibiting the IBS-M subtype. It is therefore fundamental for gastroenterologists to investigate the onset of IBS in children and adolescents with gastrointestinal complaints after an episode of acute gastroenteritis. This will help in the prevention of unnecessary referrals and the consequent substantial socioeconomic burdens. Subsequent studies are needed to explore the gastrointestinal microbiome after infection, and to provide in-depth insights into the pathogenesis of PI-IBS.

## Abbreviations

AGE	Acute gastroenteritis
CRP	C-reactive protein
IBS	Irritable bowel syndrome
IBD	Inflammatory bowel disease
LMIC	Low-to-middle-income countries
PI-IBS	Post-infection irritable bowel syndrome

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## Author contributions

SM conceived the study. SM and SD drafted the first manuscript. SM, SD, SJE, and NM aggregated and managed the raw data. SM, SD, NM, and WN critically reviewed the manuscript. All authors approved the final version of the manuscript.

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## Data availability

The data are available from the corresponding author upon reasonable request.

## Declarations

### Ethics approval and consent to participate

Ethical approval was granted by the institutional review board at Beirut Arab University (2023-H-0154-HS-R-0548) according to the Declaration of Helsinki. Written informed consent was obtained from parents or legal guardians before participation in the study.

### Consent for publication

Not applicable.

## Competing interests

The authors declare no competing interests.

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