



Original Article

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Prevalence of Gastrointestinal Symptoms in Children with COVID-19 Hospitalized at Shahid Sadoughi Hospital in Yazd

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ABSTRACT

Background: COVID-19 affects the respiratory system, but GI manifestations are recognized in children. These symptoms may precede or accompany respiratory manifestations, making their recognition important for diagnosis. This study aimed to investigate the frequency of GI manifestations and their association with characteristics and disease severity among hospitalized children with COVID-19.

Methods: This retrospective cross-sectional study included 191 children <18 years with COVID-19 hospitalized at a referral hospital in Yazd, between 2020 and 2021. Demographic, laboratory, radiological, and GI data were extracted from the COVID-19 registry and medical records. Disease severity was classified per WHO criteria. Statistical analysis was performed using the Chi-square test.

Results: Among 191 children, 78 (40.8%) had ≥ 1 GI manifestation. Common symptoms were diarrhea (26.5%), vomiting (25.4%), and abdominal pain (13.6%). No significant associations were found between GI manifestations and sex, underlying conditions, ALT levels, prognosis, ICU admission, or hospitalization length ($p > 0.05$). Nausea showed a significant association with age ($p = 0.01$), being prevalent among adolescents aged 13–16 years (16.7%), while weight loss was associated with elevated AST ($p = 0.04$). Diarrhea was the only GI symptom associated with severity, occurring more frequently in non-severe vs. severe disease (34.4% vs. 18.7%, $p = 0.01$).

Conclusion: GI manifestations are common in hospitalized children with COVID-19 and may facilitate early recognition. Although diarrhea was associated with severity, it was more frequent in non-severe cases and should not be considered an independent marker of severe illness. Severity assessment should be based on clinical presentation rather than GI manifestations alone.

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Introduction

Coronaviruses belong to the family Coronaviridae and are responsible for a variety of respiratory diseases, ranging from mild infections to severe illnesses such as severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and coronavirus disease 2019 (COVID-19)¹. The most recently discovered coronavirus that affects humans, SARS-CoV-2, emerged in December 2019 and caused a global pandemic within a short period². Although COVID-19 has primarily been known to cause a respiratory illness, it also affects multiple organ systems, as well as the gastrointestinal tract.

Although adults constitute the main population affected by COVID-19, children of all ages, including newborns, are susceptible to infection³. It has been documented that confirmed pediatric cases account for 1–8% of all infections, with most children being asymptomatic or having mild disease; however, severe presentations can occur, particularly in neonates and those with underlying comorbidities⁴. In children, respiratory symptoms are generally less severe than in adults, whereas extrapulmonary symptoms, especially gastrointestinal ones, are relatively common and may occasionally dominate the clinical picture⁵.

Gastrointestinal (GI) manifestations are a key component of COVID-19 in children. Commonly reported GI symptoms include poor appetite, nausea, vomiting, diarrhea, and abdominal pain. In some patients, these symptoms may precede respiratory manifestations or even occur in their absence^{6, 7}. The detection of SARS-CoV-2 RNA in stool samples, even after respiratory samples have tested negative, supports active viral involvement in the gastrointestinal tract. Furthermore, the expression of angiotensin-converting enzyme 2 (ACE2) receptors in intestinal epithelial cells provides a plausible biological mechanism for direct viral injury to the GI system and the resulting GI symptoms^{8, 9}.

GI symptoms are particularly prominent in

multisystem inflammatory syndrome in children (MIS-C), a hyperinflammatory condition following SARS-CoV-2 infection, and represent one of its most common clinical presentations, with abdominal pain, vomiting, and diarrhea reported in up to 71% of affected children. During the acute phase of MIS-C, elevated liver enzyme levels are observed in approximately 50% of patients, and abnormal abdominal ultrasonography findings have also been reported¹⁰.

Several studies have investigated the prevalence of GI manifestations in pediatric COVID-19. A meta-analysis by Bolia et al. identified diarrhea, nausea/vomiting, and abdominal pain as the most common GI symptoms in children with COVID-19. Other reviews have similarly confirmed frequent gastrointestinal involvement and have demonstrated associations between GI symptoms, particularly diarrhea, elevated liver enzymes, and increased disease severity^{11, 12}. Despite these findings, the reported prevalence rates vary widely among studies, and data regarding the clinical significance and outcomes of GI involvement in children remain limited.

Therefore, the aim of the present study was to evaluate the prevalence of gastrointestinal manifestations in children hospitalized with COVID-19 and to assess their association with disease severity and clinical outcomes.

Materials and Methods

Study Design and Setting

This retrospective cross-sectional study included 191 children younger than 18 years with COVID-19 hospitalized at Shahid Sadoughi Hospital, Yazd, Iran, between 2020 and 2021. Eligible patients were consecutively identified from the hospital COVID-19 registry after approval by the Ethics Committee of Shahid Sadoughi University of Medical Sciences (IR.SSU.MEDICINE.REC.1400.240).

Participants

Children younger than 18 years with a diagnosis of COVID-19 were included.

COVID-19 diagnosis was established according to the diagnostic criteria used by the hospital COVID-19 registry during the study period. Exclusion criteria included incomplete or unavailable medical records.

Data Collection

Data were extracted retrospectively from the COVID-19 patient registry and hospital medical records using a structured data collection form. The collected variables included demographic characteristics (age, sex, weight, height, and other relevant anthropometric parameters), past medical history including underlying conditions, medication history, and symptoms before hospital admission, as well as hospitalization data, including clinical manifestations with particular emphasis on gastrointestinal symptoms, findings from physical examination, vital signs, and laboratory results.

Gastrointestinal manifestations were defined as the presence of diarrhea, vomiting, nausea, abdominal pain, constipation, poor nutrition, melena, and weight loss. These symptoms were documented by treating physicians based on standard clinical definitions; for instance, diarrhea was defined as the passage of three or more loose stools per day. These variables were retrospectively extracted from the hospital COVID-19 registry and patients' medical records using a standardized data collection form. Gastrointestinal symptoms documented at hospital admission or during hospitalization by the treating physicians were included in the analysis.

Disease severity was classified according to the World Health Organization (WHO) Living Guideline for Clinical Management of COVID-19. Patients were categorized into two groups: non-severe disease, including asymptomatic, mild, and moderate illness without evidence of severe respiratory compromise; and severe disease, including severe or critical illness characterized by severe pneumonia, oxygen saturation <90% on room air, severe respiratory distress, respiratory failure requiring respiratory

support, shock, or other life-threatening organ dysfunction requiring intensive care. This classification was applied retrospectively based on the clinical information documented in the patients' medical records at the time of hospitalization.

Statistical Analysis

Data were analyzed using SPSS software version 16 (version 16, SPSS Inc., Chicago, IL). Categorical variables were compared using the Chi-square test. A $P < 0.05$ was considered statistically significant.

Results

A total of 191 hospitalized children diagnosed with COVID-19 were included in the analysis. The baseline demographic and clinical characteristics of the study population, including age, sex, underlying medical conditions, and disease severity, are presented in Table 1.

Among the 191 children, 95 (49.7%) were male, and 96 (50.3%) were female. Overall, 78 patients (40.8%) presented with at least one gastrointestinal (GI) manifestation. The most common GI symptoms were diarrhea (48 patients, 26.5%), vomiting (46 patients, 25.4%), and abdominal pain (26 patients, 13.6%), whereas melena was the least frequent manifestation (2 patients, 1.0%).

No statistically significant differences were observed in the prevalence of GI symptoms according to sex. Diarrhea was reported in 22.8% of boys and 30.3% of girls ($P = 0.25$), vomiting in 28.6% of boys and 22.2% of girls ($P = 0.32$), and poor nutrition in 11% of boys and 7.9% of girls ($P = 0.47$). Other GI manifestations also showed no significant differences based on sex ($P > 0.05$).

The frequency of GI manifestations varied across age groups, with the highest frequency observed among children aged 1 month to 1 year (38.5%) and the lowest among adolescents aged 13–16 years (11.8%); however, the overall difference was not statistically significant ($P = 0.06$). Weight loss was observed only among children aged 1–5

Table 1. Baseline Demographic and Clinical Characteristics of Hospitalized Children with COVID-19 (n = 191)

Variable	Category	Number	Percentage (%)
Age group	< 1 month	1	0.5
	1 month – 1 year	26	13.6
	1 – 5 years	59	30.9
	5 – 13 years	59	30.9
	13 – 16 years	46	24.1
Sex	Male	95	49.7
	Female	96	50.3
	Malignancy	15	7.9
	Hematologic	9	4.7
	Neurologic	25	13.1
Underlying medical conditions	Respiratory	5	2.6
	Cardiac	7	3.7
	Nephrologic	7	3.7
	Gastrointestinal	4	2.1
	Others	9	4.7
Disease severity	No underlying disease	110	57.6
	Non-severe	97	50.8
	Severe + Critical	94	49.2
ICU admission	Yes	60	31.4
	No	131	68.6
Outcome (Prognosis)	Recovered / Alive	167	87.4
	Death	24	12.6
Duration of hospitalization	≤ 7 days	141	73.8
	8 – 14 days	33	17.3
	> 14 days	17	8.9

years and 5–13 years ($P = 0.64$), while melena was reported exclusively in two children aged 1–5 years ($P = 0.34$). Vomiting was most frequent among children aged 1 month to 1 year (38.8%) and was not reported among neonates ($P = 0.42$). Nausea was significantly associated with age ($P = 0.01$), with the highest reported prevalence among adolescents aged 13–16 years (16.7%).

No significant differences were found in the prevalence of GI symptoms based on nationality. Diarrhea was reported in 27.9% of Iranian patients compared with 5.9% of non-Iranian patients ($P = 0.05$). Vomiting was reported in 26.4% of Iranian children and 23.5% of non-Iranian children ($P = 0.80$). Other GI manifestations, including weight loss and melena, were likewise similar between the two groups ($P > 0.05$).

There was no significant association between GI symptoms and alanine aminotransferase (ALT) levels. Diarrhea occurred in 18.8% of patients with normal ALT levels and in 29.3% of those with

elevated ALT levels ($P = 0.21$). As well, vomiting, nausea, weight loss, and melena showed no significant relationship with ALT levels ($P > 0.05$). No statistically significant associations were observed between aspartate aminotransferase (AST) levels and diarrhea, vomiting, nausea, or melena ($P > 0.05$). Moreover, weight loss was significantly more frequent in patients with elevated AST compared with those with normal AST (4.6% vs. 0%) ($P = 0.04$).

Diarrhea was most frequently observed in patients with underlying hematologic disorders (33.3%), followed by those with cardiac (16.7%) and neurologic (16%) conditions; however, this distribution was not statistically significant ($P = 0.41$). Weight loss was most commonly observed among patients with hematologic disorders (11.1%); however, this association was not statistically significant ($P = 0.88$). No cases of melena were reported among patients with underlying diseases. Similarly, constipation, vomiting, nausea, poor nutrition, and abdominal pain also showed no

significant associations with underlying disease categories ($P > 0.05$). The prevalence of GI manifestations in the overall population is summarized in Table 2.

Table 2. Prevalence of Gastrointestinal Manifestations in the Study Population (n = 191)

GI symptom	Number	Percentage (%)
Diarrhea	48	26.5
Vomiting	46	25.4
Abdominal pain	26	13.6
Poor nutrition	18	9.4
Nausea	12	6.3
Weight loss	4	2.1
Constipation	3	1.6
Melena	2	1.0
Any GI symptom	78	40.8

Diarrhea showed a significant association with disease severity, being reported in 34.4% of patients with non-severe disease compared with 18.7% of those with severe disease ($P = 0.01$). In contrast, no significant associations were found between disease severity and other GI manifestations, including vomiting, abdominal pain, nausea, weight loss, constipation, or melena ($P > 0.05$).

Similarly, no significant associations were found between GI manifestations and ICU

admission or length of hospitalization. The prevalence of diarrhea, vomiting, and other GI symptoms did not differ significantly among the different categories of hospital stay (≤ 7 days, 8–14 days, > 14 days) ($P > 0.05$).

Regarding chest CT findings, pleural effusion showed a significant association with diarrhea, with 21.4% of patients experiencing diarrhea demonstrating pleural effusion on chest CT ($P = 0.03$). Pleural effusion was also observed in one patient with constipation, and this association was statistically significant ($P = 0.03$). No significant associations were found between other GI manifestations and CT findings such as ground-glass opacities, atelectasis, or consolidation ($P > 0.05$).

No statistically significant associations were observed between GI symptoms and patient prognosis (survival vs. death). Although diarrhea, vomiting, and weight loss were more frequently observed among deceased patients, these differences did not reach statistical significance ($P > 0.05$ for all comparisons). The distribution of GI manifestations according to prognosis is presented in Table 3.

Table 3. Distribution of Gastrointestinal Manifestations According to Patient Prognosis

GI symptom	Category	Alive n (%)	Dead n (%)	P *
Diarrhea	No	118 (74.2)	15 (68.2)	0.54
	Yes	41 (25.8)	7 (31.8)	
Weight loss	No	163 (98.2)	24 (100)	0.50
	Yes	3 (1.8)	0 (0)	
Melena	No	165 (98.8)	24 (100)	0.59
	Yes	2 (1.2)	0 (0)	
Constipation	No	165 (98.8)	23 (95.8)	0.27
	Yes	2 (1.2)	1 (4.2)	
Vomiting	No	122 (76.7)	13 (59.1)	0.07
	Yes	37 (23.3)	9 (40.9)	
Nausea	No	159 (95.2)	22 (91.7)	0.46
	Yes	8 (4.8)	2 (8.3)	
Poor nutrition	No	144 (91.1)	19 (86.4)	0.47
	Yes	14 (8.9)	3 (13.6)	

Abdominal pain	No	144 (86.2)	21 (87.5)	0.86
	Yes	23 (13.8)	3 (12.5)	

*Chi-square test. Percentages were calculated using the number of patients with data for each specific gastrointestinal variable. The number of patients with available data varied across variables because of incomplete documentation in the medical records.

Discussion

Research has shown that only a subset of patients with COVID-19 experience gastrointestinal (GI) manifestations, with diarrhea being the most frequently reported symptom, occurring in approximately 10–50% of cases¹³. In children, GI manifestations are relatively common and include diarrhea, vomiting, abdominal pain, and nausea, which may precede, accompany, or even occur in the absence of respiratory symptoms. Rare manifestations such as acute appendicitis and liver injury, particularly in multisystem inflammatory syndrome in children (MIS-C), have also been reported, although these complications were not observed in the present study⁴.

In the present study, diarrhea, vomiting, and abdominal pain were the most common GI manifestations, whereas melena was the rarest. No significant associations were observed between GI manifestations and sex, ALT levels, underlying diseases, patient prognosis, ICU admission, or length of hospitalization. Nausea was significantly more common among adolescents aged 13–16 years, while weight loss was associated with elevated AST levels.

These findings have important clinical implications. Gastrointestinal manifestations may represent the initial or predominant presentation of SARS-CoV-2 infection in children and can occur before the onset of respiratory symptoms. Therefore, clinicians should maintain a high index of suspicion for COVID-19 in children presenting with acute gastrointestinal symptoms, particularly during periods of high community transmission. Early recognition of these manifestations may facilitate timely diagnosis, implementation of infection-control measures, and appropriate supportive management.

Several biological mechanisms may explain the gastrointestinal manifestations observed in pediatric COVID-19. SARS-CoV-2 infects intestinal epithelial cells through angiotensin-converting enzyme 2 (ACE2) receptors, which are highly expressed throughout the gastrointestinal tract. Direct viral invasion of enterocytes, together with local inflammatory responses, cytokine release, disruption of intestinal barrier integrity, and alterations of the gut microbiota, may collectively contribute to diarrhea, vomiting, and abdominal pain. Furthermore, prolonged viral shedding in stool suggests persistent gastrointestinal involvement even after resolution of respiratory symptoms.

A meta-analysis reported diarrhea, vomiting, and abdominal pain as the most common GI manifestations of COVID-19, with prevalence rates of 12.4%, 10.3%, and 5.4%, respectively¹⁴. The frequencies observed in our study were approximately twofold higher. This discrepancy may be explained by differences in hospitalization criteria, patient characteristics, geographic region, circulating SARS-CoV-2 variants, and increased clinical awareness during later phases of the pandemic. Similar to our findings, Tullie et al. reported diarrhea and vomiting as the predominant gastrointestinal manifestations among hospitalized children⁷, whereas Du et al. observed lower frequencies, possibly because their study was conducted during the early phase of the pandemic when different viral variants predominated¹⁵. Conversely, Sengul et al. reported higher rates of GI manifestations, highlighting the substantial heterogeneity among pediatric COVID-19 studies¹⁶.

Unlike Pan et al., who reported an association between gastrointestinal symptoms and prolonged hospitalization¹⁷, we found no significant relationship between individual GI

manifestations and hospital stay. This discrepancy may be explained by methodological differences, as Pan et al. analyzed gastrointestinal symptoms collectively, whereas our study evaluated each manifestation separately. Similarly, consistent with the findings of previous reports, no significant associations were observed between gastrointestinal manifestations and sex or underlying medical conditions^{18, 19}.

Notably, diarrhea demonstrated a statistically significant association with disease severity, yet it was more prevalent in non-severe cases (34.4%) than in severe cases (18.7%). This suggests that while a relationship exists, diarrhea should not be misinterpreted as an indicator of severe illness. Instead, diarrhea appears to represent a common gastrointestinal manifestation and was more frequently observed in children with non-severe disease in our study.

One possible explanation is that gastrointestinal symptoms may primarily reflect localized intestinal infection mediated by ACE2 receptor expression in enterocytes rather than the systemic inflammatory response responsible for severe pulmonary involvement. Another possible explanation is that children with severe COVID-19 tend to present predominantly with respiratory manifestations, making gastrointestinal symptoms relatively less frequent. Furthermore, the relatively small number of patients with severe disease in our cohort may have influenced the observed association.

Our findings only partially agree with previous reports. A meta-analysis by Bolia et al. identified diarrhea as the only gastrointestinal symptom associated with disease severity in pediatric COVID-19; however, unlike our findings, previous studies generally reported a higher prevalence of diarrhea among children with severe disease^{20, 21}. This discrepancy may be explained by differences in study design, patient selection, disease severity distribution, circulating SARS-CoV-2 variants, and regional epidemiological characteristics. Consequently,

diarrhea should be regarded as a common gastrointestinal manifestation of pediatric COVID-19 rather than an independent marker of disease severity.

An interesting finding of the present study was the significant association between pleural effusion and diarrhea. This observation may reflect systemic inflammation, increased vascular permeability, or fluid and electrolyte imbalance secondary to gastrointestinal losses. However, this finding should be interpreted with caution because pleural effusion was identified in only a small number of patients. Therefore, the observed association may have occurred by chance rather than representing a true pathophysiological relationship. Similarly, the association between pleural effusion and constipation should also be interpreted cautiously for the same reason. Larger multicenter studies with adequate sample sizes are needed to determine whether these associations are reproducible and clinically meaningful.

This study has several limitations that should be considered when interpreting the findings. First, it was conducted at a single referral center, which may limit the generalizability of the results to other populations and healthcare settings. Second, the relatively small sample size, particularly the limited number of patients with severe disease and pleural effusion, may have reduced the statistical power to detect associations and increased the likelihood of chance findings. Third, the retrospective design relied on information documented in medical records and the hospital COVID-19 registry, which may have resulted in incomplete documentation or information bias. Finally, although several demographic and clinical variables were evaluated, the potential influence of residual confounding factors, such as differences in treatment strategies, nutritional status, viral variants, and other unmeasured clinical characteristics, cannot be excluded. Therefore, the findings should be interpreted with caution and confirmed in larger prospective multicenter studies.

Overall, our findings support previous evidence indicating that gastrointestinal manifestations are common among hospitalized children with COVID-19 but are generally not associated with poor clinical outcomes. Recognition of gastrointestinal symptoms remains clinically important for the early identification of pediatric COVID-19. However, gastrointestinal manifestations, particularly diarrhea, should be interpreted within the overall clinical context rather than as isolated indicators of disease severity. Future prospective multicenter studies with larger sample sizes are warranted to better clarify the underlying mechanisms and prognostic significance of gastrointestinal involvement in pediatric COVID-19.

Conclusion

Gastrointestinal manifestations were commonly observed among children hospitalized with COVID-19, with diarrhea and vomiting being the most prevalent symptoms. Gastrointestinal manifestations were not associated with sex, underlying medical conditions, patient prognosis, ICU admission, or most laboratory parameters. Although diarrhea showed a statistically significant association with disease severity, its higher prevalence in non-severe cases indicates that it should not be regarded as a marker of severe illness. Consequently, diarrhea is best considered a common gastrointestinal manifestation of pediatric COVID-19, and disease severity should be assessed based on the overall clinical presentation, particularly respiratory involvement. These findings emphasize the importance of recognizing gastrointestinal manifestations in hospitalized children with COVID-19 to facilitate timely diagnosis and appropriate clinical assessment.

Conflict of Interest

The authors declare no conflict of interest.

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Ethical Considerations

This study was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences under the ethical approval code [IR.SSU.MEDICINE.REC.1400.240].

AI Disclosure

Artificial intelligence (AI)-based tools were used solely for language editing and improving the clarity and readability of the manuscript. AI tools were not used for data analysis, interpretation of results, or generation of scientific content.

Author's Contribution

Conceptualization: M. A.; Methodology: M. A. and M. K.; Data collection and analysis: M. K. and F. F.; Interpretation of results and literature review: R. E.; Manuscript drafting: S. R.; Final manuscript review and approval: M. A. and S. R.

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