

CASE REPORT



## Atypical and novel presentations of Coronavirus Disease 2019: a case series of three children

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### ABSTRACT

Typical presentations of Coronavirus Disease 2019 (Covid-19) including respiratory symptoms (cough, respiratory distress and hypoxia), fever and dyspnoea are considered main symptoms in adults, but atypical presentation in children could be a diagnostic challenge. We report three children whose initial presentation was gastrointestinal, and in whom Covid-19 infection was found, concluding that cases of acute appendicitis, mesenteric adenitis and flank tenderness may mask an infection with this virus, and should therefore be investigated.

### ARTICLE HISTORY

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### KEYWORDS

Covid-19; gastrointestinal symptoms; appendicitis; mesenteric adenitis; flank tenderness

### Introduction

The outbreak of Coronavirus Disease 2019 (Covid-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to a major global pandemic. Up to the 6<sup>th</sup> of June 2020, according to a World Health Organization (WHO) report, 6,663,304 people have been infected around the world and 392,802 (5.9%) have died [1]. SARS-CoV-2 is a single-stranded RNA virus belonging to beta coronavirus genus that enters cells via angiotensin-converting enzyme-2 (ACE-2) receptors [2]. Susceptible adults generally suffer respiratory symptoms such as pneumonia, a pathophysiology supported by damage to airway epithelial cells with secondary infiltration with inflammatory leukocytes linked to an acute phase response driving a fever [3]. Children appeared to have a milder form of the disease and typical presentations of Covid-19 also include respiratory symptoms (cough, respiratory distress), fever and dyspnoea are considered as main symptoms; however, atypical presentation mostly in children could be a concern. Although gastrointestinal symptoms including diarrhoea, vomiting and loss of appetite had been reported in adult patients with Covid-19, there are few reports of these in children. Abdominal pain and pathological features resulting in abdominal discomfort in adult Covid-19 infections are reported to be in the region of 2.2–5.8% in cohort studies [4–6].

We report the cases of prominent atypical presentation of Covid-19 in children with gastrointestinal symptoms including acute appendicitis, mesenteric adenitis

and flank tenderness. These unusual and atypical presentations have not yet been reported and so may mask an underlying infection.

### Case presentations

#### Case 1

A 10-year-old boy was referred to the emergency department with fever (39 °C), cough, headache, abdominal discomfort and vomiting without tachypnoea (normal range 14–22 breaths/min) and respiratory distress (Table 1). During hospitalization, he developed recurrent vomiting and abdominal pain with right lower quadrant tenderness presenting as an acute appendicitis. Ultrasound analysis confirmed the diagnosis of acute appendicitis. In the chest X-Ray radiography, bilateral alveolar opacity is visible in lower aspect of both lungs (Figure 1). Abdominal and pelvic CT scan was ordered by a paediatric surgeon. In cross-sectional images of lower thorax, ground glass opacity and alveolar consolidation were observed in lower lobes suggestive of Covid-19 involvement [3] (Figure 2).

In view of the respiratory findings, and with local Covid-19 cases, nasopharyngeal samples were collected and tested for SARS-CoV-2 with the LightMix® Modular Wuhan CoV RdRP-gene Kit (53–0777–96) by TIB MOLBIOL, Berlin, Germany (<https://www.roche-as.es>). Total RNA was extracted within 2 hours using a Nucleic Acid Isolation kit. The rRT-PCR assay was performed according to the manufacturer's protocol using probe P1 from the WHO

**Table 1.** Characteristics and symptoms of patients with Covid-19 infection.

Characteristics	Case 1	Case 2	Case 3
Age (years)	10	4	11
Sex	Male	Female	Female
ICU admission	Yes	Yes	No
Duration of fever	6 days	7 days	5 days
Duration of hospitalization	10 days	8 days	5 days
Cough	Yes	Yes	Yes
Diarrhoea	No	No	No
Sore throat	No	No	No
Fatigue	Yes	Yes	No
Vomiting	Yes	Yes	No
Tachopnoea	No	Yes	No
Respiratory distress	No	No	No
Hypoxaemia	No	Yes	No

protocol (RdRP\_SARSr-P1: FAM-CCAGGTGGWACRTCATC MGGTGATGC-BBQ). The positive control for rRT-PCR was an in-vitro transcribed RNA derived from strain Beta CoV\_Wuhan\_WIV04\_2019 (EPI\_ISL\_402124). The transcript contained the amplification regions of the RdRp and E gene as positive strand. rRT-PCR was performed following recommended cycling conditions: reverse transcription at 55 °C for 5 min and 95 °C for 5 min, followed by 45 cycles of PCR at 95 °C for 15 sec and 60 °C for 15 sec. Cycle threshold (Ct) value above 39.0 was considered negative. The tested sample was considered SARS-CoV-2 positive if LightMix showed positive results for the RdRP gene. A 100 bp long fragment from a conserved region of the RNA-dependent RNA polymerase (RdRP) gene was detected with a SARS-CoV-2 specific FAM labelled hydrolysis probes. In this case, a Ct-value in FAM channel <39 was defined as a positive test result. Nasopharyngeal rRT-PCR of SARS-CoV-2 was positive. Routine pathology findings were a lymphopenia, hyperglycaemia with raised CRP, ESR and creatine phosphokinase alongside marginally raised neutrophil count and creatinine (Table 2).

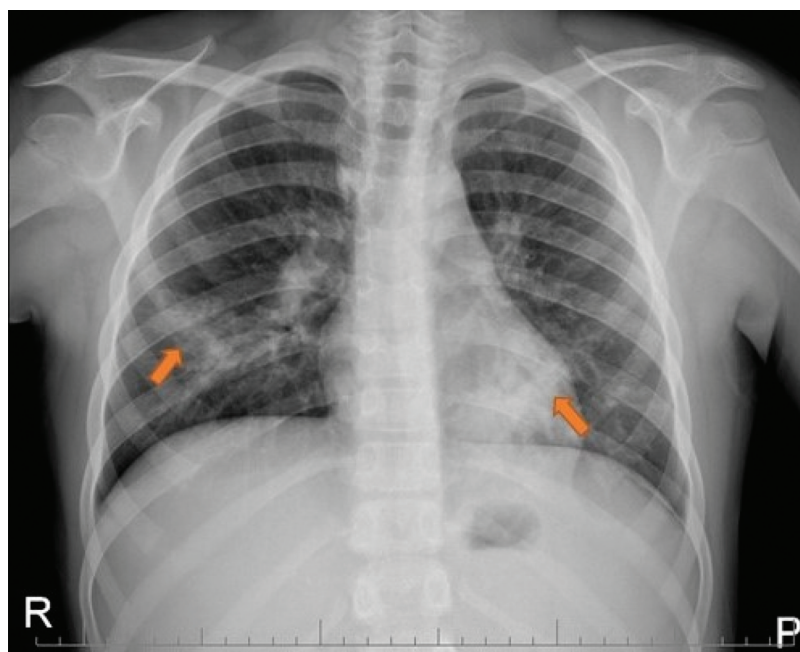
Detection of SARS-CoV-2 antibodies was performed using SARS-CoV-2 IgM ELISA kits (Pishtaz Teb, Iran, <http://pishtazteb.com>) and SARS-CoV-2 IgG ELISA kits (Pishtaz Teb, Iran <http://pishtazteb.com>) according to the manufacturer's protocol. This case was negative for both virus-specific IgG and IgM.

Azithromycin (5 mg/kg) for 5 days, cefotaxime (150 mg/kg) for 5 days, vancomycin (60 mg/kg) for 1 week, meropenem (60 mg/kg) for 1 week, hydroxychloroquine (4 mg/kg), oseltamivir (2 mg/kg) for 5 days, methylprednisolone (1.5 mg/kg) for 1 week, and intravenous immunoglobulin (IVIG) (1gr/kg) for 1 day were prescribed. The patient's clinical condition improved and he was discharged.

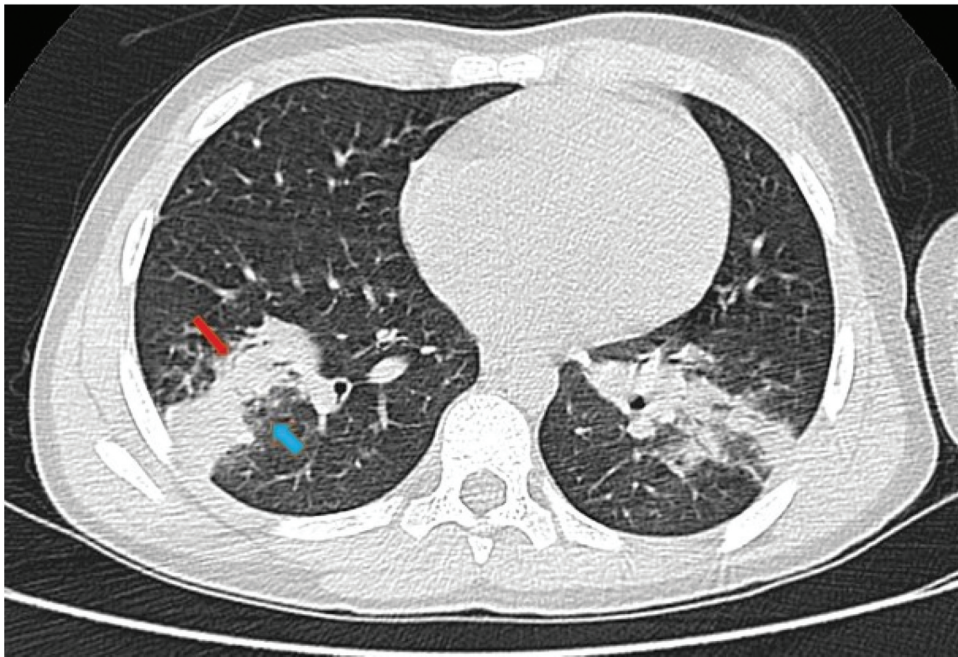
### Case 2

A 4-year-old girl was admitted to the emergency department with a 3-day history of fever (39.7 °C), abdominal pain, vomiting, malaise, headache and moderate dehydration. On examination, there was tachopnoea (normal range 20–25 breaths/min) and hypoxaemia (pulse oximetry 85% of oxygen saturation). Due to severe abdominal pain and recurrent vomiting, an ultrasound analysis was performed and acute appendicitis and multiple reactive mesenteric lymph nodes were reported. A chest X-ray showed bilateral parahilar reticular opacity, retrocardiac alveolar opacity, paracardiac alveolar opacity, retrocardiac alveolar opacity (Figure 3). Moreover, in lung view of chest CT scan, ground glass opacity and alveolar consolidation with adjacent left pleural reaction were observed (Figure 4).

Nasopharyngeal sample was collected and tested for SARS-CoV-2 with the LightMix® Modular Wuhan CoV



**Figure 1.** Chest X-Ray. Bilateral alveolar opacity is visible in lower aspect of both lungs (orange arrow) in Case 1.



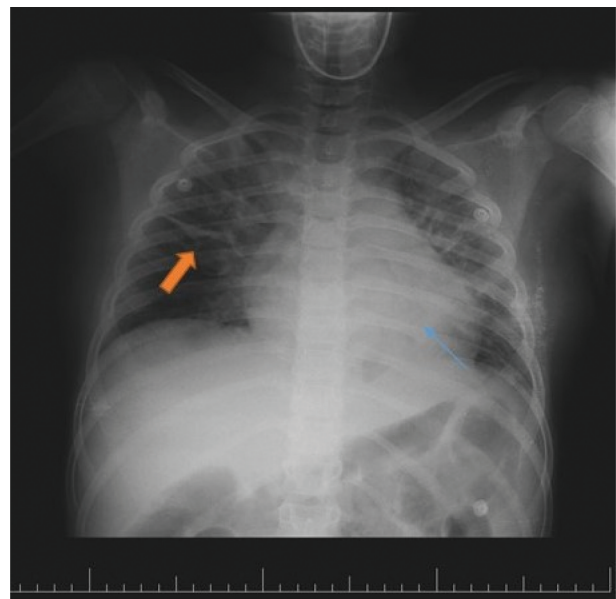
**Figure 2.** Lung view of chest CT scan from Case 1 showing ground glass opacity (blue thick arrow) and alveolar consolidation (thin red arrow) in lower lobes.

**Table 2.** Laboratory findings of patients with Covid-19 infection.

Laboratory parameters	Case 1	Case 2	Case 3	Reference range
WBCC count ( $10^9$ cells/L)	8.2	16.0	6.75	4–10
Lymphocyte count ( $10^9$ cells/L)	0.39	1.65	1.48	0.8–4
Neutrophil count ( $10^9$ cells/L)	7.1	13.6	4.8	2–7
RBCC ( $10^9$ cells/L)	4.9	4.0	4.6	3.5–5.5
Haemoglobin (g/L)	136	104	130	110–160
Platelet count ( $10^9$ cells/L)	198	195	237	150–450
Blood sugar (mg/dl)	136	78	78	70–105
Blood urea nitrogen (mg/dl)	8	17	11	5–20
Creatinine ( $\mu$ mol/L)	0.8	0.6	0.7	0.3–0.7
Sodium (mmol/L)	133	128	138	135–145
Potassium (mmol/L)	3.6	4.4	4.1	3.7–5.9
C-reactive protein (mg/L)	196	141	42	<6
Procalcitonin	0.2	0.02	0.01	<0.05
Creatine phosphokinase (U/L)	361	400	116	24–172
CPK-MB (U/L)	18	13	-	0–24
Aspartate aminotransferase (U/L)	26	27	-	10–40
Alanine aminotransferase (U/L)	21	23	-	10–40
ESR (mm/h)	31	54	22	0–10
Lactate dehydrogenase (U/L)	501	415	456	5–746

WBCC: white blood cell count. RBCC: red blood cell count: ESR: erythrocyte sedimentation rate

RdRP-gene Kit (53–0777-96) by TIB MOLBIOL, Berlin, Germany (<https://www.roche-as.es>) and Ct-value in FAM channel was <39 and defined as a positive test result. Detection of SARS-CoV-2 antibodies was performed using SARS-CoV-2 IgM ELISA kits (Pishtaz Teb, Iran, <http://pishtazteb.com>) and SARS-CoV-2 IgG ELISA kits (Pishtaz Teb, Iran, <http://pishtazteb.com>) according to the manufacturer's protocol. This case was positive for virus-specific IgG, while virus-specific IgM was not detected. The laboratory reported a leucocytosis with a neutrophilia, slightly reduced haemoglobin, and a raised creatine phosphokinase, CRP and ESR. Nasopharyngeal rRT-PCR of SARS-CoV-2 was positive in second evaluation.

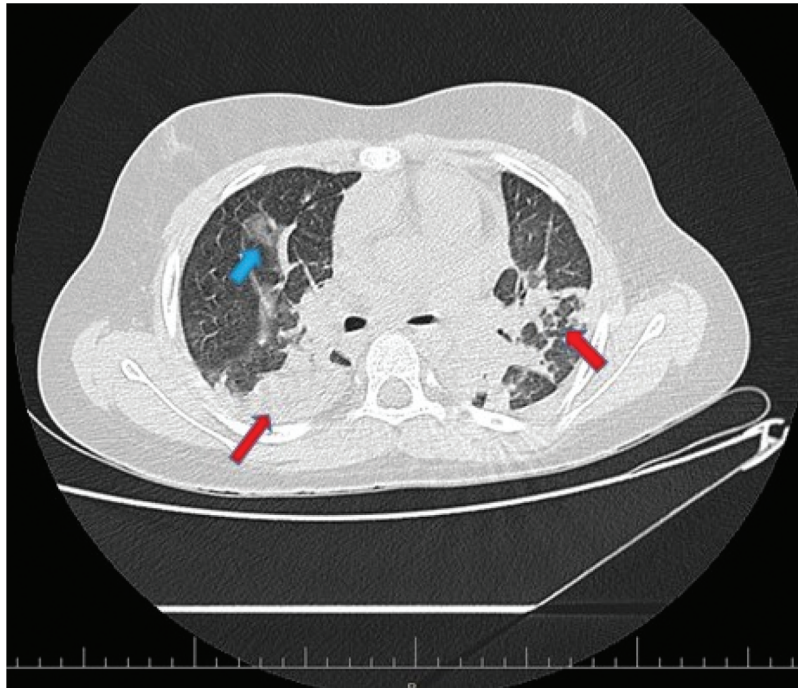


**Figure 3.** Chest X-Ray from Case 2. Bilateral parahilar reticular opacity is seen (thick orange arrow) and retrocardiac alveolar opacity in lower aspect of left lung (thin blue arrow).

Azithromycin (10 mg/kg) for 5 days, ceftriaxone (100 mg/kg) for 5 days, vancomycin (60 mg/kg) for 10 days, ceftizoxime (150 mg/kg) for 1 day, meropenem (120 mg/kg) for 10 days, metronidazole (30 mg/kg) for 1 day, and hydroxychloroquine (5 mg/kg) for 5 days were prescribed. The patient's clinical condition improved and she was discharged.

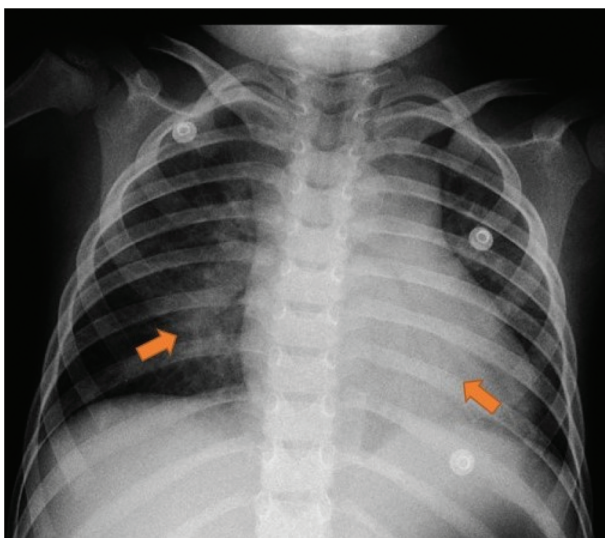
### Case 3

An 11-year-old girl was admitted to the nephrology department with costovertebral angle tenderness,



**Figure 4.** Lung view of chest CT scan from Case 2. Ground glass opacity is evident in the right upper lobe (blue arrow) and alveolar consolidation in lower lobes with adjacent left pleural reaction (red arrow).

fever and cough starting 3 days before hospitalization. She did not have any complaint regarding urinary system involvement such as dysuria, urinary retention and increased in frequency of urination. Dyspnoea, tachypnoea (normal range 14–22 breaths/min), and respiratory distress were not reported before and during her stay at hospital. Normal kidneys and mild bladder wall thickening were detected by ultrasound. A chest X-ray showed air space opacity in the lower aspect of both lungs (Figure 5). Moreover, chest CT scan showed subpleural interlobar septal thickening and alveolar consolidation in both lower lobes (Figure 6).



**Figure 5.** Chest X-Ray of Case 3. Air space opacity is visible in lower aspect of both lungs (orange arrow).

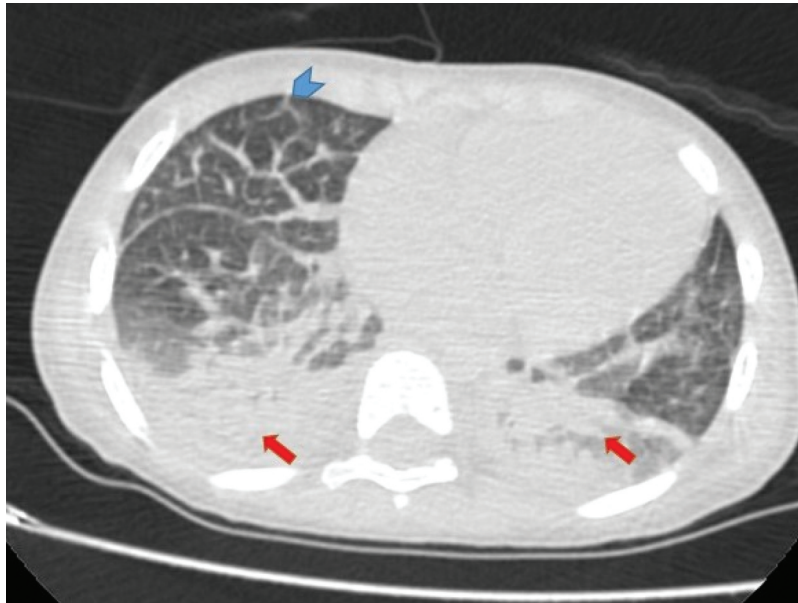
Nasopharyngeal sample was collected and tested for SARS-CoV-2 with the LightMix® Modular Wuhan CoV RdRP-gene Kit (53–0777-96) by TIB MOLBIOL, Berlin, Germany (<https://www.roche-as.es>) and Ct-value in FAM channel was <39 and defined as a positive test result. Detection of SARS-CoV-2 antibodies was performed using SARS-CoV-2 IgM ELISA kits (Pishtaz Teb, Iran, <http://pishtazteb.com>) and SARS-CoV-2 IgG ELISA kits (Pishtaz Teb, Iran, <http://pishtazteb.com>) according to the manufacturer's protocol. This case was negative for both for virus-specific IgG and IgM. The only abnormal laboratory results were raised CRP and ESR.

Oseltamivir (4 mg/kg), hydroxychloroquine (3 mg/kg), ceftriaxone (50 mg/kg) and azithromycin (5 mg/kg) for 5 days were prescribed. The patient's clinical condition improved and she was discharged.

## Discussion

There is considerable literature on adult Covid-19 infection, far in excess of that in children, possibly because symptoms are less severe and therefore not investigated, or presentation is atypical with gastrointestinal symptoms including diarrhoea, vomiting, and abdominal pain [7]. Indeed, the first case of Covid-19 in the United States was a 35-year-old man admitted with an initial presentation of nausea and vomiting followed by diarrhoea and abdominal discomfort [4]. We report paediatric cases of acute appendicitis, mesenteric adenitis and flank tenderness following Covid-19 infection.

Gastrointestinal features in Covid-19 and pathological findings of patients are discussed in detail by Tian et al. [7].



**Figure 6.** Lung view of chest CT scan from Case 3 shows sub-pleural interlobar septal thickening (blue arrow head) and alveolar consolidation in both lower lobes (red arrow).

On the basis of reviewing 2025 patients from all case reports and retrospective clinical studies regarding the digestive system involvement published since the appearance of SARS-CoV-2 outbreak. Among gastrointestinal symptoms, diarrhoea was the most frequent feature in children and adults with median duration of 4.1 days. Vomiting was observed in 3.6–16% of adults and 6.5% of children. Anorexia was detected as the most frequent gastrointestinal symptom, although its subjective nature has been impossible to evaluate completely [8]. According to a recent meta-analysis, the pooled prevalence of gastrointestinal symptoms in pediatric patients with Covid-19 was 24.8% (95% CI, 9.6–50.4) [9]. Children experience gastrointestinal symptoms more often compared with adults [10]. Only 10% of children presented with gastrointestinal symptoms at onset of disease versus 3% in adults [11,12]. As the majority of infected children with gastrointestinal symptoms are not critically ill, it may be concluded that children are more vulnerable to gastrointestinal involvement than respiratory manifestations compared to adults [13].

A case report of abdominal and testicular pain in a 42-year-old male with Covid-19 infection described no fever and respiratory manifestations at initial presentation, but a CT scan revealed ground glass opacities in lungs and mucosal thickening in the sigmoid colon [14]. In another report, a woman with acute abdominal pain suspected to cholecystitis was admitted with vomiting, anorexia, fever without any respiratory symptoms, and positive rRT-PCR of SARS-CoV-2 along with ground glass opacities in lung CT scan [15]. According to Dong *et al.* clinical manifestations in children were reported to be less serious than

adults, so that young children and infants might present only with gastrointestinal symptoms without a history of fever [16].

In our study, all three patients had positive rRT-PCR for SARS-CoV-2. Patient 2 tested positive for virus-specific IgG, while patient 1 and patient 3 were negative for both for virus-specific IgG and IgM. rRT-PCR-based viral RNA detection is sensitive and can effectively confirm early SARS-CoV2 infection. However, serological tests including those detecting IgM, or IgG antibodies are not useful for diagnosis of an acute illness because antibody response to infection takes time and it might be detectable approximately 7–11 days after exposure to the virus [17]. Our finding shows that in patient 1 and patient 3, diagnosis of SARS-CoV-2 infection was made in early phase of the infection.

Although most of the children with SARS-CoV-2 infection might present non-severe form of diseases, hyperinflammatory syndrome with multiorgan involvement similar to Kawasaki disease shock syndrome has been reported recently [18]. In addition, they may play an important role in viral transmission in the community. Prolonged shedding in nasal and faecal secretions as well as viral replication in the gastrointestinal tract is of great importance [19]. Therefore, early diagnosis of children and the implementation of effective prevention and control measures are highly recommended. We conclude that based on the present case series and other reviewed studies, global authorities should be more vigilant in atypical presentations of Covid-19, especially gastrointestinal symptoms. We recommend that Covid-19 must be considered as an equivocal presenting infection in

any patients referred to hospital with atypical presentations such as unexplained abdominal pain. This work represents an advance in biomedical science because early diagnosis of children with SARS-CoV-2 infection and the implementation of effective prevention and control measures are essential.

## Summary table

### *What is known about this subject:*

- Children appeared to have a milder form of the disease and typical presentations of Covid-19.

### *What this paper adds:*

- Three cases of prominent atypical presentation of Covid-19 in children with gastrointestinal symptoms including acute appendicitis, mesenteric adenitis and flank tenderness.

## Disclosure statement

The authors declare that they have no competing interests.

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