Faecal calprotectin in COVID-19 patients with intestinal symptoms

Walid Ismail Ellakany¹, Ahmed Mohamed AbdelHady², Mohamed Wael Nassar³, Reham Abdel Haleem Abo Elwaafa⁴

¹Tropical Medicine Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt
²Chest Diseases Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt
³Anaesthesia and Surgical Intensive Care Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt
⁴Clinical and Chemical Pathology Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt

Gastroenterology Rev 2022; 17 (4): 332–337
DOI: https://doi.org/10.5114/pg.2022.114685

Key words: COVID-19, GI symptoms, faecal calprotectin, ileocolitis.

Address for correspondence: Dr. Walid Ellakany, Tropical Medicine Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt, e-mail: walidellakany@yahoo.com

Abstract

Introduction: Extra-pulmonary manifestations of the Coronavirus disease of 2019 (COVID-19) have been increasingly reported, especially gastrointestinal and hepatic system dysfunction. The concern of faecal-oral transmission for COVID-19 was raised.

Aim: To study the trend of faecal calprotectin in COVID-19 patients with intestinal symptoms.

Material and methods: Forty confirmed cases of COVID-19 infection presenting with diarrhoea were subjected to a thorough history taking, clinical examination, and routine laboratory investigations. They were treated according to the Egyptian MOH guidelines. Faecal calprotectin (FC) concentration was measured at initial presentation and after 3 months. Those who had persistently elevated levels ≥ 200 μg/g were subjected to colonoscopic examination and histopathological examination. Forty confirmed cases of COVID-19 without diarrhoea were recruited as a control group in the initial FC evaluation.

Results: Faecal calprotectin was found to be significantly elevated in the studied COVID-19 patients who presented with diarrhoea, with a mean value 260 ±80 μg/g compared to the those without diarrhoea, with a mean value of 31.6 ±12.9 μg/g (p < 0.001). Moreover, 20% (8 patients) had an elevated level exceeding 200 μg/g 3 months after recovery; among them, 5 patients showed mild colonoscopic changes whereas 3 patients showed severe ileocolitis. Out of the 3 patients with marked ileocolitis, 2 showed histopathological changes raising the diagnosis of Crohn’s disease.

Conclusions: Faecal calprotectin was found to be elevated in COVID-19 patients with intestinal symptoms, especially diarrhoea, with or without colonoscopic and histopathological changes.

Introduction

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) is a novel coronavirus that was named after causing an outbreak in the city of Wuhan Province in China. It was named as COVID-19 by the World Health Organization after a highly contagious viral pneumonia outbreak in December 2019 and has evolved into a pandemic.

SARS-CoV2 is an enveloped, non-segmented, positive sense RNA virus. Its diameter is about 65–125 nm, containing single strands of RNA, and with crown-like spikes on the outer surface. Structurally, SARS-CoV-2 has 4 main structural proteins including spike (S) glycoprotein, small envelope (E) glycoprotein, membrane (M) glycoprotein, and nucleocapsid (N) protein, as well as several accessory proteins [1].

COVID-19 is the seventh coronavirus known to infect humans. Others include 229E, NL63, OC43, and HKU1, which only cause symptoms of the common cold and upper respiratory tract infection. Conversely, SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV) can cause atypical pneumonia [1–3].

The main clinical presentation of COVID-19 is respiratory in nature with cough, sputum expectoration, fever, and dyspnoea, which together comprise serious lower respiratory tract infection accompanied by acute respiratory distress syndrome (ARDS). Other prevalent clinical symptoms in patients with COVID-19 include
loss of taste and smell. Moreover, generalized fatigue and bone aches were evidently relevant [4].

The extrapulmonary manifestations of COVID-19 were interestingly evident in an increasing manner. This highlighted the gastrointestinal and hepatic system involvement in the course of the novel disease with an incidence of gastrointestinal symptoms higher than 20% [5].

It is known that the main route of transmission is via respiratory droplet. Extraction of SARS-CoV-2 ribonucleic acid (RNA) from the stool specimen of the first COVID-19 patient in the United States raised speculation that it could be transmitted via faeco-oral route originating from infected enterocytes of the patient’s ileum and colon [6].

All coronaviruses encode a surface glycoprotein and spike protein, which binds to host cell receptors and mediates virus entry. Betacoronavirus (β-CoVs) uses human angiotensin-converting enzyme 2 (ACE2) as an entry receptor. ACE2 is widely found in human small intestinal epithelial cells and is more strongly expressed in type II epithelial cells. Because ACE2 is highly expressed in intestinal epithelial cells, oesophagus, and lungs, coronavirus may infect the gastrointestinal tract and cause evident primary damage. Indeed, COVID patients with gastrointestinal predominant symptoms typically present with abdominal discomfort, nausea, and/or vomiting as well as severe diarrhoea with or without preceding respiratory symptoms [7, 8].

During gastrointestinal involvement for SARS-CoV-2, hepatic involvement and liver injury was noted despite the lack of expression for high-level ACE2 on hepatocytes. This was analysed by different suggestions as the high level of ACE2 expression in cholangiocytes suggests an indirect cause of elevated liver enzymes as cholangiocyte dysfunction. Also, drug hepatotoxicity as a sort of drug induced liver injury like acetaminophen was proposed. Moreover, the evident systemic inflammatory response syndrome sharing in the cytokine storm development may contribute to liver injury. Lastly, the occurrence of SARS can lead to hypoxic injury, which leads to liver dysfunction [9].

Calprotectin (aka S100A8/A9, calgranulin A and B, alarmins, CLP) is a 36.5 kD small calcium and zinc-binding heterodimer derived from neutrophils and macrophages that often associates with its main receptor, Toll-like receptor 4 (TLR4) to mediate downstream signalling with active involvement in inflammation. As an acute phase reactant, its expression level is often increased following infection, trauma, and inflammatory diseases. Faecal calprotectin represents a reliable biomarker in the context of inflammatory bowel disease, which might gain additional value during the COVID-19 pandemic [10].

**Aim**

The aim of the study was to assess faecal calprotectin as a marker of intestinal involvement in patients with COVID-19 and gastrointestinal symptoms.

**Material and methods**

The current study was carried out on 40 subjects aged from 28 to 68 years with a mean of 46.25 ±12.99 years (26 males and 24 females) during the period from July 2020 to January 2021 in Alexandria Main University Hospitals, Alexandria, Egypt. Forty COVID-19 positive patients of matched age (45.25 ±11.56 years) and sex (27 males and 23 females) without diarrhoeal presentation were recruited as a control group. The sample size was calculated using the Epi info 7 software program with a confidence level of 95% and a power of 80%. Inclusion criteria were as follows: confirmed case of COVID-19 by a nasopharyngeal and/or oropharyngeal swab real-time polymerase chain reaction (RT-PCR positive for SARS-CoV-2-RNA), and presenting with diarrhoea. Any patient with previous history of inflammatory bowel disease, lactose intolerance, celiac disease, previous history of radiation proctitis, or previous history of colorectal cancer was excluded.

Six millilitres of whole blood were collected from every subject by aseptic venepuncture from the ante-cubital vein and divided into 3 Vacutainer® tubes: the first one for CBC containing tri-potassium ethylene-diamine tetra acetic acid (K3EDTA), the second one a plain vacutainer tube to obtain serum samples for chemical analysis, and the third one a Vacutainer containing sodium citrate for D-dimer. Stool samples were collected in sterile containers for FC measurement and stool analysis.

All patients were subjected to a thorough history taking and clinical examination with stress on respiratory and intestinal stigmata of COVID-19. RT-PCR of nasopharyngeal and/or oropharyngeal swab for SARS-CoV-2-RNA was done using a VIASURE SARS-CoV-2 Real Time PCR Detection kit (CerTest BIOTEC, Spain) on a QuantStudio Real-Time PCR system (Thermo Fisher Scientific, USA) after RNA extraction with a Prepito Viral DNA/RNA kit (PerkinElmer, USA). Complete blood count (CBC) was performed on an automated cell counter ADVIA 2120 haematology system (Siemens Healthcare Diagnostics, USA). Serum ferritin, C-reactive protein (CRP), lactate dehydrogenase (LDH), alanine transaminase (ALT), and aspartate aminotransferase (AST) were automatically performed on a Dimension RxL Max Chemistry System auto analyser (Siemens Healthcare Diagnostics, USA). D-dimer was measured on a CA-1500 analyser (Siemens Healthineers, Germany). Faecal calprotectin
Variables were tested for normality using the Kolmogorov-Smirnov test. Normally distributed data were expressed using mean ± standard deviation and were compared using independent t test or one-way ANOVA. Abnormally distributed data were described using minimum, maximum, and median and were compared using the Mann-Whitney test or Kruskal-Wallis H test. Statistical significance was considered at p < 0.05.

**Results**

The most common clinical finding among the studied patients of COVID-19 was diarrhoea in 40 (100%) patients, while nausea, fever and vomiting were found in 80%, 67.5%, and 25%, respectively.

Among the selected group of patients, 26 showed a variable degree of respiratory symptoms (65%) including cough, dyspnoea, and chest tightness, whereas 29 patients showed evident CT chest changes (72.5%) (Table I).

Regarding laboratory investigations, no significant difference was detected between COVID-19 patients who presented with diarrhoea and those without diarrhoea, except for faecal calprotectin. The mean of D-dimer among the COVID-19 patients who presented with diarrhoea was 400 ±80 ng/ml compared to 430 ±73 ng/ml in patients without diarrhoea (p = 0.0837). CRP was 18 ±10 mg/l in patients with diarrhoea and 8 ±9 mg/l in patients without diarrhoea (p = 0.8148). Serum ferritin level had a mean value of 400 ±280 ng/ml in patients with diarrhoea and 460 ±270 ng/ml in those without diarrhoea (p = 0.3323). LDH, ALT, and AST showed mean values of 240 ±90 IU/l, 42 ±9.3 IU/l, and 58 ±8.5 IU/l, respectively, in patients who presented with diarrhoea versus 260 ±80 IU/l, 44 ±8.7 IU/l, and 59 ±10 IU/l, respectively, in patients without diarrhoea, with p-values of 0.2982, 0.3237, and 0.6312, respectively. Regarding white blood cell count, it showed a mean of 5.2 ±2.4 × 10^3/ml in patients with diarrhoea and 4.7 ±3.6 × 10^3/ml in patients without diarrhoea, with predominant absolute lymphopaenia in most of studied patients. The chief laboratory finding for the studied patients, especially those with a predominant severe diarrhoea having a mean 260 ±80 μg/g (Table II). Faecal calprotectin was measured in 40 COVID-19 patients without diarrhoeal presentation and showed a mean value of 31.6 ±12.9 μg/g compared to 80 ±260 μg/g in those with diarrhoeal presentation (p < 0.001).

**Ethics approval and consent to participate**

The proposal of the current study was approved by the Ethical Committee of the Faculty of Medicine-Alexandria University, Alexandria, Egypt. Written informed consent was signed by all participants or their caregivers before the study. The committee’s reference number is not available. The current study is original and has not been published elsewhere in any form or language (partially or in full). The results of the current study are presented honestly and without fabrication, falsification, or inappropriate data manipulation. No data, text, or theories by others are presented as if they were the author’s own (‘plagiarism’).

**Statistical analysis**

Data were analysed using IBM SPSS software package version 20.0. The distributions of quantitative variables were tested for normality using the Kolmogorov-Smirnov test. Normally distributed data were expressed using mean ± standard deviation and were compared using independent t test or one-way ANOVA. Abnormally distributed data were described using minimum, maximum, and median and were compared using the Mann-Whitney test or Kruskal-Wallis H test. Statistical significance was considered at p < 0.05.

**Results**

The most common clinical finding among the studied patients of COVID-19 was diarrhoea in 40 (100%) patients, while nausea, fever and vomiting were found in 80%, 67.5%, and 25%, respectively.

Among the selected group of patients, 26 showed a variable degree of respiratory symptoms (65%) including cough, dyspnoea, and chest tightness, whereas 29 patients showed evident CT chest changes (72.5%) (Table I).

Regarding laboratory investigations, no significant difference was detected between COVID-19 patients who presented with diarrhoea and those without diarrhoea, except for faecal calprotectin. The mean of D-dimer among the COVID-19 patients who presented with diarrhoea was 400 ±80 ng/ml compared to 430 ±73 ng/ml in patients without diarrhoea (p = 0.0837). CRP was 18 ±10 mg/l in patients with diarrhoea and 8 ±9 mg/l in patients without diarrhoea (p = 0.8148). Serum ferritin level had a mean value of 400 ±280 ng/ml in patients with diarrhoea and 460 ±270 ng/ml in those without diarrhoea (p = 0.3323). LDH, ALT, and AST showed mean values of 240 ±90 IU/l, 42 ±9.3 IU/l, and 58 ±8.5 IU/l, respectively, in patients who presented with diarrhoea versus 260 ±80 IU/l, 44 ±8.7 IU/l, and 59 ±10 IU/l, respectively, in patients without diarrhoea, with p-values of 0.2982, 0.3237, and 0.6312, respectively. Regarding white blood cell count, it showed a mean of 5.2 ±2.4 × 10^3/ml in patients with diarrhoea and 4.7 ±3.6 × 10^3/ml in patients without diarrhoea, with predominant absolute lymphopaenia in most of studied patients. The chief laboratory finding for the studied patients, especially those with a predominant severe diarrhoea having a mean 260 ±80 μg/g (Table II). Faecal calprotectin was measured in 40 COVID-19 patients without diarrhoeal presentation and showed a mean value of 31.6 ±12.9 μg/g compared to 80 ±260 μg/g in those with diarrhoeal presentation (p < 0.001).

**Ethics approval and consent to participate**

The proposal of the current study was approved by the Ethical Committee of the Faculty of Medicine-Alexandria University, Alexandria, Egypt. Written informed consent was signed by all participants or their caregivers before the study. The committee’s reference number is not available. The current study is original and has not been published elsewhere in any form or language (partially or in full). The results of the current study are presented honestly and without fabrication, falsification, or inappropriate data manipulation. No data, text, or theories by others are presented as if they were the author’s own (‘plagiarism’).

**Statistical analysis**

Data were analysed using IBM SPSS software package version 20.0. The distributions of quantitative variables were tested for normality using the Kolmogorov-Smirnov test. Normally distributed data were expressed using mean ± standard deviation and were compared using independent t test or one-way ANOVA. Abnormally distributed data were described using minimum, maximum, and median and were compared using the Mann-Whitney test or Kruskal-Wallis H test. Statistical significance was considered at p < 0.05.

**Results**

The most common clinical finding among the studied patients of COVID-19 was diarrhoea in 40 (100%) patients, while nausea, fever and vomiting were found in 80%, 67.5%, and 25%, respectively.

Among the selected group of patients, 26 showed a variable degree of respiratory symptoms (65%) including cough, dyspnoea, and chest tightness, whereas 29 patients showed evident CT chest changes (72.5%) (Table I).

Regarding laboratory investigations, no significant difference was detected between COVID-19 patients who presented with diarrhoea and those without diarrhoea, except for faecal calprotectin. The mean of D-dimer among the COVID-19 patients who presented with diarrhoea was 400 ±80 ng/ml compared to 430 ±73 ng/ml in patients without diarrhoea (p = 0.0837). CRP was 18 ±10 mg/l in patients with diarrhoea and 8 ±9 mg/l in patients without diarrhoea (p = 0.8148). Serum ferritin level had a mean value of 400 ±280 ng/ml in patients with diarrhoea and 460 ±270 ng/ml in those without diarrhoea (p = 0.3323). LDH, ALT, and AST showed mean values of 240 ±90 IU/l, 42 ±9.3 IU/l, and 58 ±8.5 IU/l, respectively, in patients who presented with diarrhoea versus 260 ±80 IU/l, 44 ±8.7 IU/l, and 59 ±10 IU/l, respectively, in patients without diarrhoea, with p-values of 0.2982, 0.3237, and 0.6312, respectively. Regarding white blood cell count, it showed a mean of 5.2 ±2.4 × 10^3/ml in patients with diarrhoea and 4.7 ±3.6 × 10^3/ml in patients without diarrhoea, with predominant absolute lymphopaenia in most of studied patients. The chief laboratory finding for the studied patients, especially those with a predominant severe diarrhoea having a mean 260 ±80 μg/g (Table II). Faecal calprotectin was measured in 40 COVID-19 patients without diarrhoeal presentation and showed a mean value of 31.6 ±12.9 μg/g compared to 80 ±260 μg/g in those with diarrhoeal presentation (p < 0.001).
In the follow-up profile 3 months after recovery, 8 patients previously diagnosed with severe gastrointestinal COVID-19 (20%) had an elevated level of faecal calprotectin exceeding 200 μg/g.

The main gastrointestinal sequelae observed in the COVID-19 patients after 3 months of recovery, using 2 consecutive negative RT-PCR tests from nasopharyngeal swabs, were persistent diarrhoea (75%), mucorrhoea (50%), abdominal discomfort/distention (75%), and bleeding per rectum (12.5%) (Table III).

Among the 8 patients with a persistently elevated faecal calprotectin exceeding 200 μg/g, 5 showed mild colonoscopic changes in the form of mild erythematous rectal erythema that showed a non-specific form of rectosigmoiditis (12.5%), whereas 3 patients showed severe ileocolitis revealed endoscopically as atrophic villi, aphthoid ileal ulceration, and marked rectosigmoiditis (7.5%).

Out of the 3 previously diagnosed patients with marked ileocolitis induced by COVID-19, 2 patients showed a histopathological diagnosis of additive cryptitis, crypt abscess, and crypt distortion involving lymphoplasmocytic and neutrophilic infiltration raising the diagnosis of Crohn’s disease (5%).

### Discussion

The first evidence of excretion of SARS-CoV-2 RNA in a stool specimen was in the first reported COVID-19 patient in the United States [6]. Recently, it has become well-known that some COVID-19 patients have gastrointestinal manifestations as the presenting or the main symptom in the course of the disease [12–14]. Although diarrhoea and other gastrointestinal symptoms are frequent in COVID-19 patients, the significance remains undetermined [15, 16]. In the same context, diarrhoea was a frequent symptom in severe acute respiratory syndrome (SARS) patients (40%). Intestinal affection was associated with worse disease outcomes. In Middle East respiratory syndrome (MERS), despite the same observation of frequent occurrence of diarrhoea (14% to 50% of cases), a less severe fate of the disease was associated with gastrointestinal symptoms [17–20].

The question is raised from such a study: Does COVID-19 infection trigger intestinal dysbiosis or alter the immunological responses that may lead to inflammatory bowel disease?

Zhang et al. isolated SARS-CoV-2 RNA in oral swabs, anal swabs, and blood, and concluded that infected subjects can shed the virus in respiratory, faecal-oral, or body fluid routes [21]. Xiao et al. found 39 (53.4%) patients to be positive for COVID-19 in stool for 1 to 12 days, with 17 patients of them persisting to have positive stool specimens even after a negative PCR in their respiratory specimens [22]. Wong et al. found

---

**Table II.** Laboratory findings of the studied COVID-19 patients with and without diarrhoea

| Laboratory parameters | Laboratory values in COVID-19 patients with diarrhoea (n = 40) n (%) | Laboratory values in COVID-19 patients without diarrhoea (n = 40) n (%) | t  | P-value |
|-----------------------|-------------------------------------------------------------------|-------------------------------------------------------------------|----|---------|
| CRP [mg/dl]           | 8.5 ±10                                                           | 8 ±9                                                             | 0.235 | 0.8148 |
| D-dimer [ng/ml]       | 400 ±80                                                           | 430 ±73                                                          | 1.752 | 0.0837 |
| Leukocytes [× 10^9/ml]| 5.2 ±2.4                                                          | 4.7±3.6                                                          | 0.731 | 0.4670 |
| Lymphocytes [× 10^9/ml]| 1 ±0.7                                                           | 1.2 ±0.9                                                         | 1.109 | 0.2707 |
| Ferritin [ng/ml]      | 400 ±280                                                          | 460 ±270                                                         | 0.976 | 0.3323 |
| LDH [IU/l]            | 240 ±90.5                                                         | 260 ±80                                                          | 1.047 | 0.2982 |
| AST [IU/l]            | 58 ±8.5                                                           | 59 ±10                                                           | 0.482 | 0.6312 |
| ALT [IU/l]            | 42 ±9.3                                                           | 44 ±8.7                                                          | 0.993 | 0.3237 |
| Faecal calprotectin [μg/g] | 80 ±260                                                         | 12.9 ±31.6                                                      | 18.169 | < 0.001* |

* – Student’s t-test, p – p-value for comparing between the studied groups. *Statistically significant at p ≤ 0.05.

**Table III.** Three-month follow-up findings of the studied COVID-19 patients with diarrhoea

| Follow up findings | COVID-19 patients with diarrhoea (n = 40) n (%) |
|--------------------|-----------------------------------------------|
| 3-month faecal calprotectin ≥ 200 μg/g | 8 (20%) |
| Colonoscopy changes: | |
| Minimal* | 5 (12.5%) |
| Severe** | 3 (7.5%) |
| Pathological diagnosis of IBD | 2 (5%) |

*Minimal colonoscopic changes: non-specific mild rectosigmoiditis. **Severe ileocolonoscopic changes: atrophic ileal villi with aphthoid ulcerations, marked erythema of rectosigmoid. IBD – inflammatory bowel disease (both patients were pathologically diagnosed as having Crohn’s disease).
8 children persisting to be positive on rectal swabs even after nasopharyngeal negativity for the virus [23].

The faecal calprotectin (FC) measurement may play a crucial role in the diagnosis and in the monitoring of COVID-19-related diarrhoea because SARS-CoV-2 causing an inflammatory response in the intestine was clearly shown by elevated measured levels, and this was correlated with elevated serum IL-6 levels [24, 25].

In our cohort of COVID-19 patients, there was a higher percentage of males (64% vs. 36%). This concurs with the results of many published articles and reviews [26–33]. The mean age of our patients was 49.6 ±9 years. Effenberger et al. reported the mean age of patients without diarrhoea, patients with ceased diarrhoea (> 48 h), and patients with acute diarrhoea (< 48 h) as 58.4 ±17.1, 66.3 ±13.1, and 78.3 ±13.8 years, respectively [24]. Ai et al. studied 7 COVID-19 patients with gastrointestinal symptoms as their initial or main symptoms and persistent for more than 3 days, and they found the age ranging from 35 to 75 years [13].

Many of our patients had fever at presentation (67.5%). In a systematic review published in March 2020, Li et al. reported fever as the most frequent presenting symptom in 88.5% of Chinese patients (83.0% to 100%) [26]. Later, Kim et al. published in April 2020 that fever was present in only 11.6% of South Korean mild COVID-19 patients [29]. Yang et al. found fever in 171 patients out of 200 hospitalized patients outside Wuhan (85.5%) [28]. Goyal et al. found fever in 25.5% of patients in New York City [32]. Al-Omari et al. found fever in 36.2% of non-intensive care unit COVID-19 Saudi Arabian patients [30].

All our study patients had elevated presenting FC (260 ±80 µg/g). Effenberger et al. also found significantly elevated FC in their group of patients with ceased diarrhoea, and to a larger extent in patients with ongoing diarrhoea, compared with patients without diarrhoea (p < 0.001). However, they did not find SARS-CoV-2-RNA in stools from patients with ongoing diarrhoea, and this was only detected in 8 patients with ceased diarrhoea and in 4 patients without diarrhoea, but there was no relation between faecal SARS-CoV-2-RNA and other biomarkers (FC, IL-6, CRP, or ferritin) [24]. Unfortunately, we could not investigate for detection of faecal viral RNA because of the local non-availability of the technique.

In the same direction, Ojetti et al. presented very interesting data regarding the significant correlation between COVID-19 pneumonia and high level of faecal calprotectin (expression of gastrointestinal involvement) in patients with COVID-19 infection. The presence of pneumonia is an expression of the disease’s severity [34]. Similar results were reported by several studies [35, 36].

Lin et al. stated that 6 patients who underwent endoscopic examination that identified SARS CoV-2 RNA showed histopathological changes of numerous infiltrating plasma cells and lymphocytes as well as interstitial oedema in the lamina propria, in accordance with the current study in which 5 patients showed mild colonicoscopic changes in the form of mild erythematous rectal erythema, which showed a non-specific form of rectosigmoiditis, whereas 3 patients had marked ileocolitis induced by COVID-19, and 2 patients showed a histopathological diagnosis of additive cryptitis, crypt abscess, and crypt distortion involving lymphoplasmocytic and neutrophilic infiltration [37].

On the contrary, Xiao et al. found that among a cohort of 73 patients, no abnormalities were observed in the stomach, duodenum, colon, and rectum, with the exception of mucosa damage in the oesophagus at endoscopy [22].

Moreover, Liu et al. raised the interest of small intestinal involvement in an 85-year-old man with a segmental dilatation alternating with stenosis with COVID-19 autopsy despite its colour being normal. Whether this finding is secondary to COVID-19 or a pre-existent GI comorbidity such as ischaemia remains unknown [27].

Our data suggest that faecal calprotectin is elevated in COVID-19 patients with intestinal symptoms, especially diarrhoea with or without colonscopic and histopathological changes. Whether the expression of SARS-COV-2 receptors in the GI tract is related to calprotectin levels or COVID-19 only exacerbates pre-existing chronic inflammatory changes remains to be further illustrated in future larger-scale studies.

Acknowledgments

We sincerely thank all patients and healthy subjects for their cooperation in the current study. We acknowledge the Molecular Biology Research lab team in the Medical Research Centre, Alexandria Faculty of Medicine. We also thank Eng. Amgad Hamza for revising the statistical analysis of the results.

Conflict of interest

The authors declare no conflict of interest.

References

1. Phelan A, Katz R, Gostin L. The novel coronavirus originating in Wuhan, China and challenges for Global Health Governance. JAMA 2020; 323: 709-10.
2. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. Classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol 2020; 5: 536-44.
3. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in coronavirus disease 2019 patients. Int J Infect Dis 2020; 94: 91-5.

4. Guan W, Ni Z, Hu Y, et al. Clinical characteristics of Coronavirus disease 2019 in China. N Engl J Med 2020; 382: 1708-20.

5. Borges I, Cacic N, Abdulazeem H, et al. Novel Coronavirus infection (COVID-19) in humans. J Clin Med 2020; 9: 13-9.

6. Holshue M, DeBolt C, Lindquist S, et al. First case of 2019 novel Coronavirus in the United States. N Engl J Med 2020; 382: 929-36.

7. Zhou Z, Zhao N, Shu Y, et al. Effect of gastrointestinal symptoms on patients infected with Coronavirus disease 2019. Gastroenterology 2020; 12: 17-9.

8. Tian Y, Rong L, Nian W, He Y. Gastrointestinal features in COVID-19 and the possibility of faecal transmission. Aliment Pharmacol Ther 2020; 51: 843-51.

9. Bangash MN, Patel J, Parekh D. COVID-19 and the liver. Lancet 2020; 395: 994-1001.

10. Ai JW, Zi H, Wang Y, et al. Clinical characteristics of COVID-19 patients in China. Front Med 2020; 7: 308.

11. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in coronavirus disease 2019 patients. Int J Infect Dis 2020; 94: 91-5.

12. Huang C, Wang Y, Li X, et al. Clinical features of patients in China with severe acute respiratory syndrome 2019-nCoV infection. J Med Virol 2020; 92: 1543-4.

13. Wang G, Chen W, Jin X, Chen YP. Description of COVID-19 cases along with the measures taken on prevention and control in Zhejiang, China. J Med Virol 2020; 92: 1948-55.

14. Yang L, Liu J, Zhang R, et al. Epidemiological and clinical features of 200 hospitalized patients with coronavirus disease 2019 outside Wuhan, China: a descriptive study. J Clin Virol 2020; 129: 104475.

15. Kim GU, Kim MJ, Ra SH, et al. Clinical characteristics of asymptomatic and symptomatic patients with mild COVID-19. Clin Microbiol Infect 2020; 26: 948.e1-3.

16. Al-Omari A, Alhuqbani WN, Zaidi ARZ, et al. Clinical characteristics of non-intensive care unit COVID-19 patients in Saudi Arabia: a descriptive cross-sectional study. J Infect Public Health 2020; 13: 1639-44.

17. Thevarajan I, Busing KL, Cowie BC. Clinical presentation and management of COVID-19. Med J Aust 2020; 213: 134-9.

18. Goyal P, Choi JJ, Pinheiro LC, et al. Clinical characteristics of Covid-19 in New York City. N Engl J Med 2020; 382: 2372-4.

19. Fu L, Wang B, Yuan T, et al. Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: a systematic review and meta-analysis. J Infect 2020; 80: 656-65.

20. Ojetti V, Saviano A, Covino M, et al.; GEMELLI AGAINST COVID-19 group. COVID-19 and intestinal inflammation: role of fecal calprotectin. Dig Liver Dis 2020; 52: 1231-33.

21. Zhang W, Du RH, Li B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. Emerg Microbes Infect 2020; 9: 386-9.

22. Xiao F, Tang M, Zheng X, et al. Evidence for gastrointestinal infection of SARS-CoV-2. Gastroenterology 2020; 158: 1831-3.

23. Wong SH, Lui RN, Sung JJ. Covid-19 and the digestive system. J Gastroenterol Hepatol 2020; 35: 744-8.

24. Effenberger M, Grabbherr F, Mayr L, et al. Faecal calprotectin indicates intestinal inflammation in COVID-19. Gut 2020; 69: 1543-4.

25. Mazza S, Sorce A, Peyvandi F, et al. A fatal case of COVID-19 pneumonia occurring in a patient with severe acute ulcerative colitis. Gut 2020; 69: 1148-9.

26. Li Q, Huang T, Wang YQ, et al. COVID-19 patients’ clinical characteristics, discharge rate, and fatality rate of meta-analysis. J Med Virol 2020; 92: 577-83.

27. Yang L, Liu J, Zhang R, et al. Epidemiological and clinical features of 200 hospitalized patients with coronavirus disease 2019 outside Wuhan, China: a descriptive study. J Clin Virol 2020; 129: 104475.

28. Al-Omari A, Alhuqbani WN, Zaidi ARZ, et al. Clinical characteristics of non-intensive care unit COVID-19 patients in Saudi Arabia: a descriptive cross-sectional study. J Infect Public Health 2020; 13: 1639-44.

29. Thevarajan I, Busing KL, Cowie BC. Clinical presentation and management of COVID-19. Med J Aust 2020; 213: 134-9.

30. Goyal P, Choi JJ, Pinheiro LC, et al. Clinical characteristics of Covid-19 in New York City. N Engl J Med 2020; 382: 2372-4.

31. Fu L, Wang B, Yuan T, et al. Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: a systematic review and meta-analysis. J Infect 2020; 80: 656-65.

32. Ojetti V, Saviano A, Covino M, et al.; GEMELLI AGAINST COVID-19 group. COVID-19 and intestinal inflammation: role of fecal calprotectin. Dig Liver Dis 2020; 52: 1231-33.

33. Shokri-Afraf A, Alkilani A, Moradiipoosh B, et al. Elevated fecal and serum calprotectin in COVID-19 are not consistent with gastrointestinal symptoms. Sci Rep 2021; 11: 22001.

34. Jin B, Singh R, Ha SE, et al. Pathophysiological mechanisms underlying gastrointestinal symptoms in patients with COVID-19. World J Gastroenterol 2021; 27: 2341-52.

35. Lin L, Jiang X, Zhang Z, et al. Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection. Gut 2020; 69: 997-1001.

Received: 10.11.2021
Accepted: 18.01.2022