Gastrointestinal and hepatic abnormalities in patients with confirmed COVID-19: A systematic review and meta-analysis

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Respiratory symptoms of COVID-19 including fever, dry cough, and dyspnea are the most common manifestations of this novel infectious disease, similar to severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). Although other manifestations such as gastrointestinal symptoms are less common, the initial presentation of the disease in some patients was gastrointestinal symptoms. Different studies have reported various prevalence rates for gastrointestinal symptoms such as diarrhea in patients with COVID-19.

Knowing the frequency and characteristics of these manifestations of COVID-19 is important for both clinicians and health policy makers.
A systematic review and meta-analysis of the available data on the gastrointestinal and liver manifestations of patients with COVID-19 was performed.

PubMed and Scopus databases and Google Scholar search engine were searched for published and unpublished preprint articles up to 10 April 2020.

Original studies providing information on clinical digestive symptoms or biomarkers of liver function in patients with PCR confirmed diagnosis of COVID-19 were included.

After quality appraisal, data were extracted.
No language limitations were imposed. Different combinations of the following search terms were used:

“Gastrointestinal” OR “Digestive” AND “Liver” OR “Hepatic”, AND “Coronavirus Disease 2019.” For each term, all synonyms and subjects with the same heading were also searched.

To minimize the risk of bias, studies that were conducted exclusively on a specific population and were not representative of the whole range of manifestations (eg, studies only on children, severe and critical cases, fatal cases, etc) were also excluded.
Initial search retrieved 1036 records from different sources. After removing duplicates, 675 records were screened via title and abstract review.

Having excluded the irrelevant studies, the full text articles of 124 records were reviewed, of which 57 were excluded due to noncompliant design, insufficient data, or nonstandard diagnostic methods.
Characteristics of the included studies, including first author, study design, publication date, origin, sample size, and quality assessment score, as well as population type and patient demographics including sex and age are extracted.
67 studies were included in this systematic review and meta-analysis, comprising a pooled population of 13,251 patients with confirmed COVID-19.

The most common gastrointestinal symptoms were anorexia (10.2%, 95% confidence interval [CI] = 6.2%-16.4%), diarrhea (8.4%, 95% CI = 6.2%-11.2%), and nausea (5.7%, 95% CI = 3.7%-8.6%), respectively.

Decreased albumin levels (39.8%, 95% CI = 15.3%-70.8%), increased aspartate aminotransferase (22.8%, 95% CI = 18.1%-28.4%), and alanine aminotransferase (20.6%, 95% CI = 16.7%-25.1%) were common hepatic findings.

After adjusting for preexisting gastrointestinal (5.9%) and liver diseases (4.2%), the most common gastrointestinal findings were diarrhea (8.7%, 95% CI = 5.4%-13.9%), anorexia (8.0%, 95% CI = 3.0%-19.8%), and nausea (5.1%, 95% CI = 2.2%-14.3%).
| Findings                  | All studies (published and preprint) | Published studies |
|--------------------------|-------------------------------------|-------------------|
|                          | N patients | N studies | Point estimate (%) | 95% CI (%) | $I^2$ | N patients | N studies | Point estimate (%) | 95% CI (%) | $I^2$ |
| **Gastrointestinal symptoms** |            |          |                  |            |       |            |          |                  |            |       |
| Anorexia                 | 3871       | 15       | 10.2             | 6.2-16.4   | 95.65 | 2590       | 11        | 16.2             | 10.3-24.5 | 94.83 |
| Diarrhea                 | 10 452     | 56       | 8.4              | 6.2-11.2   | 93.80 | 7101       | 41        | 8.6              | 6.8-10.8  | 83.07 |
| Nausea                   | 50 89      | 23       | 5.7              | 3.7-8.6    | 88.08 | 3740       | 19        | 7.2              | 4.7-10.9  | 87.31 |
| Vomiting                 | 45 67      | 20       | 3.8              | 2.5-5.9    | 81.80 | 3434       | 18        | 4.6              | 3.0-6.8   | 78.57 |
| Abdominal pain           | 23 42      | 10       | 3.2              | 2.1-4.7    | 44.17 | 2267       | 9         | 3.3              | 2.2-4.9   | 46.97 |
| Abdominal distension     | 12 17      | 3        | 1.1              | 0.2-5.6    | 78.76 | 84         | 1         | 3.6              | 1.2-10.5  | 0.00  |
| **Liver function abnormalities** |            |          |                  |            |       |            |          |                  |            |       |
| Decreased albumin        | 50 5        | 7        | 39.8             | 15.3-70.8  | 94.77 | 505        | 7         | 39.8             | 15.3-70.8  | 94.77 |
| Elevated AST             | 20 62       | 16       | 22.8             | 18.1-28.4  | 83.05 | 1910       | 14        | 22.4             | 17.2-28.5  | 84.31 |
| Elevated ALT             | 14 96       | 8        | 20.6             | 16.7-25.1  | 65.63 | 1282       | 5         | 20.3             | 15.2-26.6  | 78.12 |
| Elevated PT              | 32 3        | 3        | 180              | 30-60.8    | 97.03 | 248        | 2         | 83               | 3.7-17.3   | 63.90 |
| Elevated TBIL            | 14 29       | 9        | 7.8              | 5.0-12.0   | 72.02 | 1354       | 7         | 68               | 4.1-11.0   | 72.64 |
| Elevated ALP             | 26 3        | 2        | 4.6              | 2.6-7.9    | <0.01 | 263        | 2         | 4.6              | 2.6-7.9    | <0.01 |
| **Preexisting diseases** |            |          |                  |            |       |            |          |                  |            |       |
| Digestive disease        | 11 52       | 9        | 5.9              | 4.1-8.5    | 51.73 | 861        | 6         | 5.9              | 3.7-9.2    | 58.31 |
| Liver disease            | 58 91       | 30       | 4.2              | 3.3-5.3    | 56.74 | 5207       | 24        | 4.3              | 3.3-5.6    | 61.84 |

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; COVID-19, coronavirus disease-2019; PT, prothrombin time; TBIL, total bilirubin.
| Findings                  | All studies (published and preprint) | Published studies |
|---------------------------|--------------------------------------|-------------------|
|                           | N patients  | N studies | Point estimate (%) | 95% Cl (%) |  \(i^2\) | N patients  | N studies | Point estimate (%) | 95% Cl (%) |  \(i^2\) |
| Gastrointestinal symptoms |                                      |                   |
| Diarrhea                  | 5104        | 23        | 8.7                | 5.4-13.9   | 94.62   | 2308        | 15         | 9.9                | 6.5-14.9   | 85.90   |
| Anorexia                  | 2515        | 5         | 8.0                | 3.0-19.8   | 97.21   | 1438        | 3          | 20.0               | 9.5-37.2   | 95.97   |
| Nausea                    | 2458        | 7         | 5.1                | 2.3-11.0   | 88.63   | 1349        | 4          | 8.1                | 4.0-15.6   | 70.30   |
| Vomiting                  | 2513        | 6         | 3.7                | 1.6-8.3    | 85.29   | 1577        | 5          | 5.8                | 3.3-10.2   | 71.67   |
| Abdominal pain            | 1400        | 3         | 3.7                | 2.8-4.8    | <0.01   | 1400        | 3          | 3.7                | 2.8-4.8    | <0.01   |
| Abdominal distension      | 1020        | 2         | 0.7                | 0.0-18.9   | 89.22   | 84          | 1          | 3.6                | 1.2-10.5   | 0.00    |
| Liver function abnormalities |                                      |                   |
| Decreased albumin         | 136         | 2         | 49.3               | 34.4-64.4  | 48.41   | 136         | 2          | 49.3               | 34.4-64.4  | 48.41   |
| Elevated ALT             | 426         | 3         | 19.4               | 9.9-34.3   | 88.68   | 364         | 2          | 20.8               | 8.3-43.4   | 93.71   |
| Elevated AST             | 311         | 3         | 15.2               | 9.3-23.8   | 59.98   | 311         | 3          | 15.2               | 9.3-23.8   | 59.98   |

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; COVID-19, coronavirus disease-2019.
## Table 4

Pooled prevalence of gastrointestinal symptoms, preexisting diseases, and liver function abnormalities in patients with different severities of COVID-19

| Findings                  | Nonsevere |          |          |          |          |          | Severe |          |          |          |          |
|---------------------------|-----------|----------|----------|----------|----------|----------|--------|----------|----------|----------|----------|
|                           | N patients| N studies| Point estimate (%) | 95% CI (%) | $\hat{r}$ | N patients| N studies| Point estimate (%) | 95% CI (%) | $\hat{r}$ |
| **Gastrointestinal symptoms** | | | | | | | | | | | |
| Anorexia                  | 502       | 5        | 14.9     | 7.6-27.2 | 84.92    | 208      | 5        | 31.4     | 12.4-59.7 | 91.49    |
| Diarrhea                  | 2006      | 11       | 5.5      | 3.5-8.4  | 71.67    | 535      | 10       | 11.1     | 6.7-18.0  | 69.02    |
| Nausea                    | 326       | 3        | 9.5      | 3.0-26.2 | 89.24    | 148      | 3        | 9.5      | 5.7-15.4  | <0.01    |
| Vomiting                  | 326       | 3        | 2.5      | 0.7-9.2  | 59.59    | 148      | 3        | 5.1      | 2.4-10.3  | <0.01    |
| Abdominal pain            | 350       | 3        | 1.8      | 0.8-4.0  | <0.01    | 148      | 3        | 8.1      | 4.5-14.0  | <0.01    |
| Abdominal distension      | 142       | 1        | 2.1      | 0.7-6.3  | <0.01    | 55       | 1        | 1.8      | 0.3-11.8  | <0.01    |
| **Liver function abnormalities** | | | | | | | | | | | |
| Decreased albumin         | 94        | 2        | 27.2     | 6.2-67.9 | 66.39    | 42       | 2        | 80.2     | 44.1-95.4 | 72.81    |
| Elevated AST              | 1265      | 8        | 11.6     | 7.2-18.0 | 81.77    | 355      | 8        | 36.7     | 30.0-43.9 | 34.97    |
| Elevated ALT              | 1039      | 4        | 15.0     | 8.5-25.2 | 89.27    | 253      | 4        | 30.8     | 25.0-37.3 | 88.1     |
| Elevated TBIL             | 918       | 3        | 7.5      | 4.7-11.7 | 59.33    | 217      | 3        | 17.3     | 11.4-25.4 | 39.20    |
| Elevated ALP              | 324       | 2        | 0.1      | 0.01-8.7 | 56.97    | 89       | 2        | 5.7      | 0.7-32.4  | 71.40    |
| **Preexisting diseases**  |          |          |          |          |          |          |        |          |          |          |          |
| Digestive disease         | 281       | 3        | 5.2      | 3.1-8.6  | <0.01    | 133      | 3        | 6.9      | 1.9-22.3  | 69.18    |
| Liver disease             | 1781      | 8        | 3.2      | 1.8-5.7  | 69.94    | 488      | 8        | 4.9      | 2.4-9.5   | 50.32    |
Funnel plot of studies reporting anorexia in the primary unadjusted meta-analysis
Funnel plot of studies reporting diarrhea, after adjusting for preexisting diseases
Gastrointestinal and liver manifestations are not rare in patients with COVID-19, but their prevalence might be affected by preexisting diseases.

Diarrhea, anorexia and mild liver abnormalities seem to be relatively common in COVID-19, regardless of comorbidities.
Ethics approval and consent to participate

The study was approved by the Ethics Committee of Mashhad University of Medical Sciences.

Competing interests

The authors declare that they have no competing interests.