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Gastroenterological and hepatic manifestations of patients with COVID-19, prevalence, mortality by country, and intensive care admission rate: systematic review and meta-analysis

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ABSTRACT

Background and aims Patients infected with the SARS-CoV-2 usually report fever and respiratory symptoms. However, multiple gastrointestinal (GI) manifestations such as diarrhoea and abdominal pain have been described. The aim of this study was to evaluate the prevalence of GI symptoms, elevated liver enzymes and mortality of patients with COVID-19.

Methods A systematic review and meta-analysis of published studies that included a cohort of patients infected with SARS-CoV-2 were performed from 1 December 2019 to 15 December 2020. Data were collected by conducting a literature search using PubMed, Embase, Scopus, and Cochrane according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. We analysed pooled data on the prevalence of individual GI symptoms and elevated liver enzymes and performed subanalyses to investigate the relationship between GI symptoms/elevated liver enzymes, geographical location, mortality, and intensive care unit (ICU) admission.

Results The available data of 78 798 patients positive for SARS-CoV-2 from 158 studies were included in our analysis. The most frequent manifestations were diarrhoea (16.5%, 95% CI 14.2% to 18.4%), nausea (9.7%, 95% CI 9.0% to 13.2%) and elevated liver enzymes (5.6%, 95% CI 4.2% to 9.1%). The overall mortality and GI mortality were 23.5% (95% CI 21.2% to 26.1%) and 3.5% (95% CI 3.1% to 6.2%), respectively. Subgroup analysis showed non-statistically significant associations between GI symptoms/elevated liver enzymes and ICU admissions (OR=1.01, 95% CI 0.55 to 1.83). The GI mortality was 0.9% (95% CI 0.5% to 2.2%) in China and 10.8% (95% CI 7.8% to 11.3%) in the USA.

Conclusion GI symptoms/elevated liver enzymes are common in patients with COVID-19. Our subanalyses showed that the presence of GI symptoms/elevated liver enzymes does not appear to affect mortality or ICU admission rate. Furthermore, the proportion of GI mortality among patients infected with SARS-CoV-2 varied based on geographical location.

INTRODUCTION

In December 2019, China was faced with a new strain of coronavirus, novel coronavirus (2019 nCov). Within a short period of time, it manifested into a full pandemic.[1] It was first noticed by the innumerable cases of pneumonia that suddenly surged among local inhabitants in the province of Wuhan.[2] Soon, the virus was detected through sequencing, leading to it officially being renamed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses.[3] The disease caused by SARS-CoV-2 was allocated the title of COVID-19 or 'coronavirus disease'.[3] Coronaviruses in general are single-stranded RNA viruses falling under the family of Coronaviridae, which also include Middle East respiratory syndrome coronavirus (MERS Cov) and SARS (SARS-CoV).[4] By the end of December 2020, more than 81 million cases of COVID-19 have officially been confirmed worldwide, and mortality from COVID-19 was more than 1 798 050 deaths worldwide.[5] In addition, new variants of SARS-CoV-2 have been discovered in the UK, South Africa, and other regions around the world.[6]

It has been established that the transmission of SARS-CoV-2 occurs from person to person through the upper airway tract (droplet infection) or through direct contact.[7] The virus can also be detected in saliva, urine, gastrointestinal (GI) tract and possibly through airborne spread.[8 9] The spectrum of symptoms attributable to SARS-CoV-2 includes fever, cough, myalgia, fatigue, and, to a lesser extent, headache. Patients may also be asymptomatic.[10–12] Diarrhoea, nausea and vomiting, as well as liver involvement have all been

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reported in the literature.[13 14] In fact, GI involvement is plausible, given that ACE2, the major human cellular receptor for the SARS-CoV-2, is expressed in the GI tract, as well as in liver cells.[15] We thus conducted a systematic review of published GI symptoms and elevated liver enzymes associated with COVID-19 on the basis of disease severity, mortality, intensive care unit (ICU) admission, and geographical region. This will aid in understanding the magnitude of involvement of the GI tract and liver in patients with COVID-19.

METHODS

Search strategy

A systematic review was conducted using PubMed, Scopus, Cochrane, and Embase databases. Medical literature searches for human studies were performed from 1 December 2019 up to 15 December 2020. The key terms used for the literature search were ((“COVID-19” OR “COVID 2019” OR “severe acute respiratory syndrome coronavirus 2” OR “severe acute respiratory syndrome coronavirus 2” OR “2019 nCoV” OR “SARS-COV2” OR “2019nCoV” OR (“severe acute respiratory syndrome coronavirus 2” OR “SARS-COV2” AND “gastrointestinal” AND (“manifestations” OR “clinical characteristics”) OR (“gastrointestinal tract” OR (“gastrointestinal’ AND “tract”) OR “gastrointestinal tract” OR (“gi” AND “tract”) OR (“fatality” or “Mortality”). In addition, a manual search of all review articles, editorials and retrieved original studies was also performed. All procedures used in this meta-analysis were consistent with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and prespecified protocol, which described our method and analysis before data collection was initiated (see online supplemental material PRISMA checklist).

Selection criteria and data extraction

Data were independently extracted by two investigators (MS and FA) and any discrepancies between the two authors were resolved through discussion. Inclusion and exclusion criteria were defined prior to the literature search. The inclusion criteria were (1) study type: case reports/case series (including chart reviews), prospective/retrospective cohort studies, case–control studies, cross-sectional studies and randomised controlled trials; (2) patient population: adult patients with COVID-19, inpatient or outpatient setting; and (3) outcome measured: at least one reported GI symptom or elevated liver enzyme, number of patients admitted to ICU, and number of deaths reported. In addition, systematic reviews and meta-analyses were also reviewed for any relevant studies.

For the purpose of this study, elevated liver enzyme defined as aspartate aminotransferase (AST) or alanine aminotransferase (ALT) value above the upper limit of normal of each study laboratory reference range. Furthermore, overall mortality was defined as the proportion of deaths among identified confirmed COVID-19 cases in all studies that reported it. The number of deaths among patients experiencing GI symptoms/elevated liver enzymes was extracted and referred to as GI mortality.

Exclusion criteria were (1) review, opinion, abstracts from conferences, editorials, commentary articles, and review articles; (2) studies without data for retrieval; (3) duplicate studies; (4) asymptomatic patients with COVID-19; and (5) studies that did not report GI symptoms.

Data extraction was performed using Microsoft Excel. The following data were extracted:

1. Study: author, journal, date, country, number of patients, and study type.
2. Patients characteristics: mean age, ethnicity, gender, and comorbidities.
3. Number of reported deaths in all studies.
4. Number of patients admitted to the ICU.
5. Number of patients who experienced the following GI symptoms/elevated liver enzymes: abdominal pain, diarrhoea, nausea, anorexia, loss of taste, AST or ALT above the upper limit of normal of each study laboratory reference range.

Risk of bias and certainty of evidence

The Methodical Index for Non-randomized Studies (MINORS)[16] was used to assess bias risk. In addition, risk of bias was assessed based on four domains: selection, ascertainment, causality, and reporting. An overall judgement of risk of bias was made based on factors deemed to be most critical for the systematic review (selection criteria, ascertainment of outcome, and follow-up duration).

Statistical analysis

Our primary analysis focused on assessing the weighted pooled prevalence of GI symptoms/elevated liver enzymes in patients with COVID-19 infection, occurring any time during the course of illness. We also conducted subanalyses that looked at the association between GI symptoms/elevated liver enzymes and mortality as well as ICU admission. Categorical variables were described as count (%). Continuous variables were described using mean (SD) if they are normally distributed, median (IQR) if they are not. We pooled the single-arm event rates using a random effects method, and we measured heterogeneity within our studies using the I^2 statistic. Subanalyses were described and tested using ORs and 95% CIs to determine statistical significance. STATA V.16 was used to calculate ORs and their respective 95% CI and to create Forest and box plots.

Sensitivity analysis

To examine the effect of the quality of studies on our results, we performed a sensitivity analysis on the prevalence of GI symptoms/elevated liver enzymes by excluding low-quality studies. To do so, we used the modified Newcastle-Ottawa Quality Assessment Scale for non-randomised studies.[17] A study with a score of 0–3

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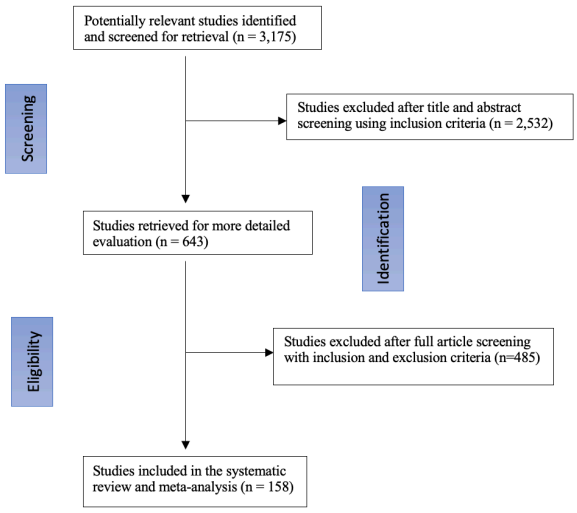

Figure 1 Flow diagram for study selection.

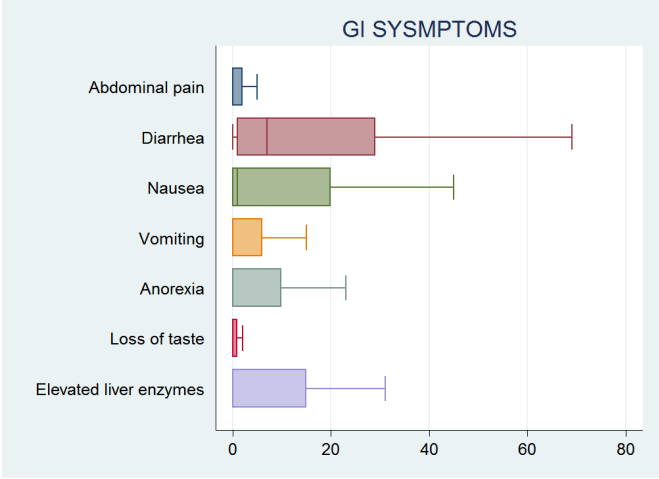

Figure 2 Box plots showing the distribution and proportion of GI symptoms/elevated liver enzymes in patients with COVID-19. GI, gastrointestinal.

was classified as a low-quality study. On the other hand, studies that scored 4 or above were included in the analysis.

RESULTS

Research selection and quality assessment

Overall, 158 studies (online supplemental table 1) from 3175 potentially relevant citations were included in the analysis (figure 1). Most of the included studies were single arm only; very few studies included comparator groups. Furthermore, outcome assessors in all 158 studies were not blinded. Both inpatient and outpatient studies were included. The risk of evidence imprecision was rated as very serious, given that the included studies were all observational studies. Overall, all included studies were rated as having very serious risk of bias because they lacked a control group and had a high risk of confounding and selection bias (online supplemental table 2).

Clinical data

This systematic review included 158 studies[2–4 8 12–14 16 18–147] with a total of 78 798 patients that tested positive for SARS-CoV-2 and were included in the analysis. The mean patient age was 55.6 years (±14, 95% CI 48 to 57.3) and 45.2% of the patients were men. Most patients had several comorbidities, the most common being hypertension (28.7%, 95% CI 21.3% to 29.1%), diabetes mellitus (17.4%, 95% CI 13.0% to 19.2%), and cardiovascular diseases (15.7%, 95% CI 13.3% to 17.1%). GI symptoms included nausea, vomiting, abdominal pain, loss of taste, anorexia and diarrhoea (figure 2). Heterogeneity statistic I^2 is 95%, which signifies a significant heterogeneity among our studies. The most common reported manifestation among GI symptoms/elevated liver enzymes was diarrhoea (online supplemental figure 1). Specifically, GI symptoms/elevated liver enzymes of patients infected with SARS-CoV-2 are diarrhoea (16.5%, 95% CI 14.2% to 18.4%), nausea (9.7%, 95% CI 9.0% to 13.2%), anorexia or loss of appetite (1.6%, 95% CI 1.2% to 5.1%), vomiting (1.5%, 95% CI 5.1% to 8.0%), abdominal pain (4.5%, 95% CI 3.1% to 7.3%), loss of taste (1.3%, 95% CI 1.1% to 4.1%), and elevated liver enzymes (5.6%, 95% CI 4.2% to 9.1%) (online supplemental table 3).

Sensitivity analysis

The sensitivity analysis included 52 studies (online supplemental tables 4 and 5). The results did not differ from our main analysis. Among the GI manifestations experienced by patients with COVID-19, diarrhoea (16.6%, 95% CI 12.1% to 17.3%) was still the most common symptom, followed by nausea (9.9%, 95% CI 8.2% to 11.7%). The proportion of patients experiencing loss of taste was 4.7% (95% CI 3.8% to 5.9%). The percentage of patients experiencing elevated liver enzymes was 1.9% (95% CI% 1.3% to 3.4%).

Mortality and geographical variation

A total of 83 studies reported mortality. Of those, 82 studies reported mortality as the number of deaths at the time of the study. Only one study reported mortality as death over 30 days.[143] The overall prevalence of overall mortality and GI mortality were 23.5% (95% CI 21.2% to 26.1%) and 3.5% (95% CI 3.1% to 6.2%), respectively (online supplemental tables 6 and 7). The subgroup analysis included eight studies[19 20 57 110 136 139 141 143] that directly compared the number of deaths in patients with and without GI symptoms/elevated liver enzymes. In this analysis, the number of patients who experienced GI symptoms/elevated liver enzymes and those who did not were 1593 and 3321, respectively. The results showed that patients with GI symptoms/elevated liver enzymes were not more likely to die compared with those who did not, with a statistically insignificant pooled odds of patients of 1.01 (95% CI 0.46 to 2.25) (figure 3).

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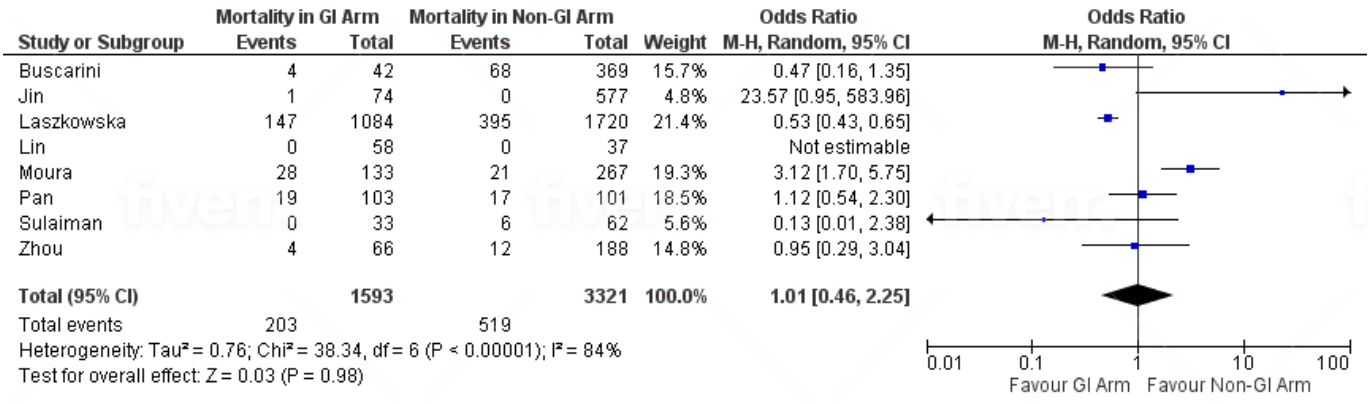

Figure 3 Forest plot of GI mortality in patients with COVID-19, showing no significant difference in the pooled odds of patients with GI symptoms/elevated liver enzymes and those without. GI, gastrointestinal.

Moreover, out of the 158 studies, a total of 42 studies reported mortality in patients with GI symptoms/elevated liver enzymes based on their geographical location (figure 4). This analysis showed that 44 out 4946 patients (0.9%) in China died (95% CI 0.5 to 2.2), whereas 192 out 1783 patients (10.8%) in the USA died (95% CI 7.8 to 11.3). In addition, 2 out of 9 patients (22.2%) in Italy died, while 28 out of 400 patients (7%) in Brazil died. Furthermore, three studies from Taiwan, Korea, and Japan reported zero GI mortality (table 1).

ICU admission rate

Five studies[22 85 139 141 148] reported differences in ICU admissions among patients manifesting GI symptoms/elevated liver enzymes and patients who did not. The total number of patients with GI symptoms/elevated liver enzymes who were admitted to the ICU was 1282, and the number of patients who did not experience GI symptoms/elevated liver enzymes and were admitted to the ICU was 2512. No statistically significant difference in

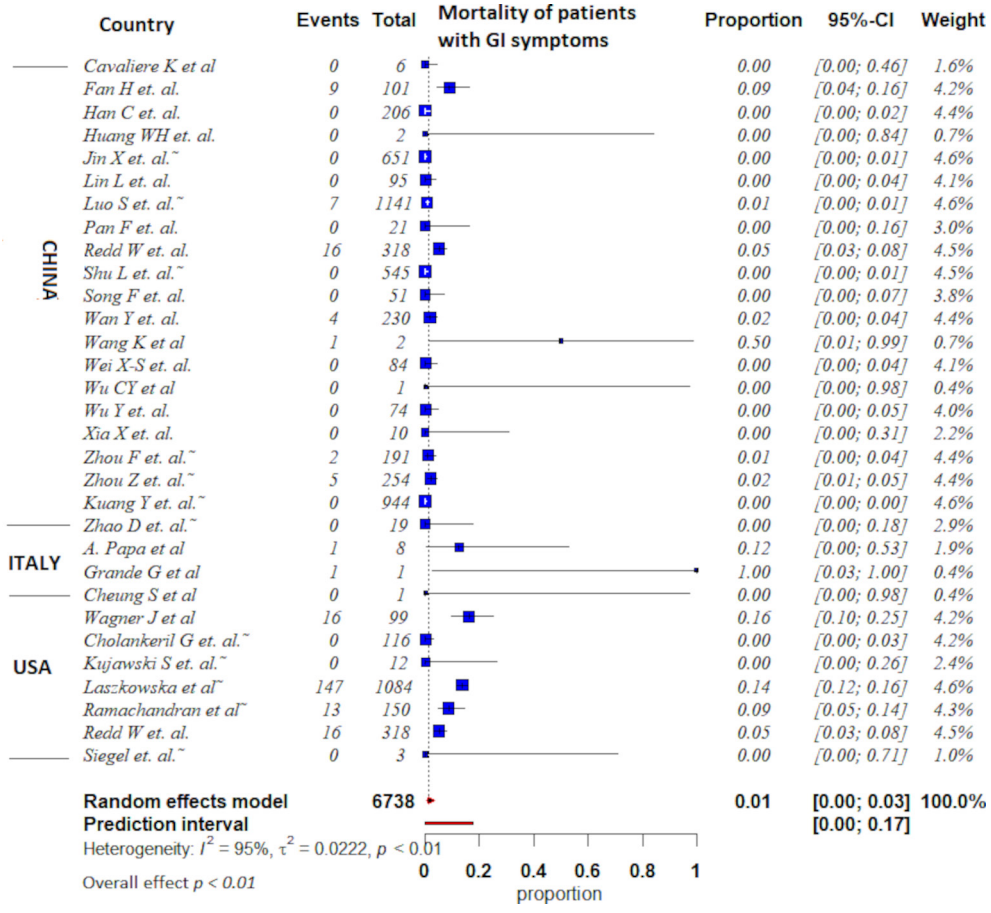

Figure 4 Forest plot of GI mortality in patients with COVID-19 who are experiencing GI symptoms/elevated liver enzymes in three different countries. GI, gastrointestinal.

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Table 1 GI mortality by geographical location

Study	Patients (total n)	Mortality in patients with GI symptoms	Country
Fan *et al*[48]	101	9	China
Han *et al*	206	0	China
Huang *et al*	2	0	China
Kuang *et al*	944	0	China
Shu *et al*	545	0	China
Jin *et al*	651	0	China
Lin *et al*	95	0	China
Pan *et al*	21	0	China
Zhao *et al*	19	0	China
Redd *et al*	318	16	China
Luo *et al*	1141	7	China
Song *et al*	51	0	China
Wan *et al*	230	4	China
Wei *et al*	84	0	China
Wu *et al*	74	0	China
Zhou *et al*	191	2	China
Zhou *et al*	254	5	China
Xia *et al*	10	0	China
Cavaliere *et al*	6	0	China
Wu *et al*	1	0	China
Wang *et al*	2	1	China
Total China	4946	44	0.9%
Ramachandran *et al*	150	13	USA
Wagner *et al*	99	16	USA
Cheung *et al*	1	0	USA
Cholankeril *et al*	116	0	USA
Kujawski *et al*	12	0	USA
Redd *et al*	318	16	USA
Siegel *et al*	3	0	USA
Laszkowska *et al*	1084	147	USA
Total USA	1783	192	10.8%
Grande *et al*	1	1	Italy
Papa *et al*	8	1	Italy
Total Italy	9	2	22.2%
Hsih *et al*	2	0	Taiwan
Tabata *et al*	104	0	Japan
Moura *et al*	400	28	Brazil (7%)
Wahab *et al*	1	0	Denmark
Dietrich *et al*	1	0	Germany
Kandasamy *et al*	1	0	India
Sulaiman *et al*	140	0	Iraq
Hassani *et al*	2	1	Iran
Khader *et al*	1	0	Qatar
Gulen *et al*	1	0	Turkey
Kim *et al*	28	0	South Korea

ICU admission rate was noted between those who experienced GI symptoms/elevated liver enzymes and those who did not. The pooled proportion was 1.01 (95% CI 0.55 to 1.83) (figure 5).

DISCUSSION

This meta-analysis of 78 798 patients with COVID-19 found that GI symptoms/elevated liver enzymes are common in patients infected with SARS-CoV-2. Subgroup analysis found that no association between the presence of GI symptoms/elevated liver enzymes and mortality or ICU admission, which is similar to the finding of other meta-analyses.[149 150]

GI symptoms including abdominal pain, diarrhoea, nausea, vomiting, loss of appetite, loss of taste and elevated liver enzyme are among the presenting symptoms or laboratory abnormalities of SARS-CoV-2 infection found in this study. Diarrhoea was the most common GI symptom; this is particularly important because previous studies have shown that patients with diarrhoea on presentation have a higher stool RNA positivity and viral load than those without.[22 36 151] One study showed that 44 of 153 patients with COVID-19 tested positive for the virus in the stools.[148] In addition, a report of a patient with COVID-19 with positive faecal but negative pharyngeal and sputum viral tests has been described.[33] Moreover, a meta-analysis concluded that SARS-CoV-2 is commonly present in stool samples or anal swabs in which the virus can persist for a long period after respiratory samples become negative and that the virus may be viable.[152] This may imply that faecal oral route is a possible route of SARS-CoV-2 transmission.

The possibility of faecal oral transmission of SARS-CoV-2 emphasises the importance of frequent and proper hand hygiene. This is important in every clinical setting, but especially in low-resource areas with poor sanitation.[38] Intuitively, proper handling of the excreta of patients with COVID-19 should still be strongly enforced, and sewage from hospitals should also be properly disinfected. The presence of the virus in the digestive tract also raises the concerns of COVID-19 infection in patients with established GI conditions, as well as potential faecal microbiota transplant donors.[148] Nevertheless, the unknown effect of COVID-19 on patients with pre-existing GI diseases and its influence on treatment and outcome is a cause for concern. These implications warrant further investigation. The American Gastroenterological Association and joint society recommend the use of enhanced personal protective equipment, including the use of N95 (or N99) masks instead of surgical masks, for healthcare workers performing upper or lower GI procedures regardless of COVID-19 status.[35]

It is believed that the prevalence of GI symptoms is underestimated because the majority of studies included in our study reported GI symptoms only on the day of admission but not throughout the disease course. Furthermore, many earlier studies did not report on

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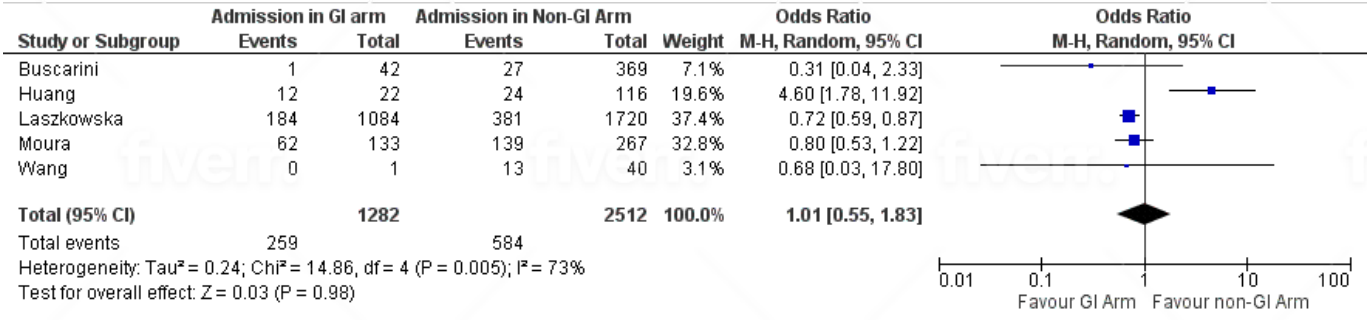

Figure 5 Forest plot showing odd ratio (OR) of intensive care unit admissions in patients with COVID-19 with and without GI symptoms/elevated liver enzymes. GI, gastrointestinal.

other GI symptoms except for diarrhoea.[22] Based on these findings, clinicians must be aware that digestive symptoms, such as diarrhoea, may be a presenting feature of COVID-19 that can arise before respiratory symptoms and, on rare occasions, may be the only presenting manifestation of COVID-19.[33]

The pooled analysis showed that the overall mortality and GI mortality were 23.5% and 3.5%, respectively. However, it is important to emphasise that reporting of COVID-19 mortality in each country varies.[153] Some countries do not depend on the availability of confirmed laboratory tests; instead, both probable and confirmed cases are used when calculating COVID-19 mortality.[154]

In this meta-analysis, a subanalysis of mortality in patients with GI symptoms/elevated liver enzymes varied between countries. This difference in GI mortality can be attributed to several reasons. Differences in reporting cases, case definition, and the mortality measure used might have a great role in this geographical variation. The available mortality data mostly reported as case fatality rate, which measures the number of deaths out of all confirmed cases.[155] Furthermore, using case fatality rate is influenced by reporting and testing strategies in each country, where countries that do not have good reporting or intensive testing might miss a lot of confirmed cases and eventually overestimate mortality.[153] In addition, it is well known that comorbidities increase the risk of death from COVID-19,[154] and countries with the highest burden of chronic diseases had the highest COVID-19 mortality. Small sample size of the published GI mortality reports of some countries is another factor that can lead to inaccurate presentation of the actual GI mortality.

Our study did not show higher GI mortality among patients manifesting GI symptoms/elevated liver enzymes. However, any possible true difference in mortality may be worth further investigation among better defined patients with COVID-19 subgroups with GI symptoms/elevated liver enzymes because one study showed that prevalence of severe disease was more common in patients who had GI symptoms than those who did not.[156] Our meta-analysis did not find a statistically significant association between patients with GI symptoms/elevated liver enzymes and ICU admission. However, to investigate such an association, it is important to consider other causes of elevated liver enzymes in patients admitted to ICU such as sepsis, hypoperfusion, hepatotoxic drugs, and parenteral nutrition.[157]

Strengths and limitations

Our study has several strengths. This is one of the more recent meta-analyses that summarises the literature on COVID-19 and the prevalence of overall and individual GI manifestations.[149 158–161] The large patient population and comprehensive inclusion of 158 studies allow a more precise estimation of the prevalence of GI symptoms/elevated liver enzymes associated with COVID-19. Moreover, our search included studies over 1-year period, from 1 December 2019 up to 15 December 2020, which makes it more up-to-date and more inclusive of the recent evidence. Furthermore, our meta-analysis included studies from different countries and regions.

This study, however, is subject to some limitations. Most of the studies we base our analyses on are observational, single-arm cohorts. The lack of control groups and comparison arms can lead to bias due to confounding. Additionally, regarding mortality among patients with COVID-19, most studies reported mortality at the time of the study. In other words, studies did not report mortality over a specific period of time. Furthermore, most studies reported patients with COVID-19 who have been admitted to hospital, who are more likely to have severe disease, resulting in under-representation of patients with milder disease.

CONCLUSION

In this meta-analysis, we summarise the recent reports of GI symptoms/elevated liver enzymes among patients infected with SARS-CoV-2. GI symptoms/elevated liver enzymes are commonly observed in patients with COVID-19; therefore, clinicians should be aware that diarrhoea and nausea can be the only manifestations of patients with COVID-19. Our subanalysis showed that GI mortality among patients infected with SARS-CoV-2 varied based

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on geographical location. We also could not find a statistically significant association between ICU admission in patients with GI symptoms/elevated liver enzymes compared with those without GI symptoms/elevated liver enzymes. However, further investigation is warranted to better assess this possible association.

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Supplemental Material

Table. 1. Studies included in the meta-analysis

Study	Journal	Study type	Date	Country
Siegel et al	American Roentgen Ray Society	Case series	Apr-20	USA
Pazgan-simon et al	Polish Archives of Internal Medicine	Case report	Apr-20	Poland
Yang, X et al	Clinics and Research in Hepatology and Gastroenterology	Case report	Apr-20	China
Zhang, J et al	Allergy (John Wiley and Sons Ltd.)	Retrospective cohort study	Feb-20	China
Azwar et al	Indones J Intern Med	Case report	Jan-20	Indonesia
Jin, X et al	BMJ	Retrospective cohort study	Mar-20	China
Nobel et al	Gastroenterology	Case-Control Study	Apr-20	USA
Lin et al	BMJ	Retrospective cohort study	Mar-20	China
Zhou et al	Gastroenterology	Retrospective cohort study	Mar-20	China
Pan et al	The American Journal of GASTROENTEROLOGY	Cross-sectional study	Apr-20	China
Poggiali et al	European Journal of Case Reports in Internal Medicine	Case series	Mar-20	Italy
Cholankeril et al	Gastroenterology	Retrospective cohort study	Apr-20	USA
Fu et al	Digestive Diseases and Sciences (Springer)	Case report	Apr-20	China
Li et al	World Journal of Clinical Cases	Case report	Apr-20	China
Saeed et al	British Journal of Surgery	Retrospective cohort study	Apr-20	Norway
Arashiro et al.	Journal of travel medicine	case-report	Apr-20	Japan
Yang F et al	Journal Of Medical Virology	Retrospective Cohort Study	Apr-20	China
Guillen, E et al	American Journal of Transplantation	Case Report	Mar-20	Spain
Chen, Y et al	Journal Of Medical Virology	Retrospective Cohort Study	Apr-20	China
Chen Q et al	Journal of Medical Virology	SHORT COMMUNICATION	Mar-20	China
Huang et al	The Lancet	Prospective Cohort study	Fab-20	China
Chen, N et al	The Lancet	Retrospective Cohort Study	Fab-20	China
Wang et al	JAMA	Case series	Mar-20	China
Xu, X et al	BMJ	retrospective case series	Fab-20	China
Fan et al	MedRxiv	Retrospective Cohort Study	Fab-20	China
Zhang, B et al	MedRxiv	Retrospective Cohort Study	Fab-20	China

Study	Journal	Study type	Date	Country
Huang Y et al	MedRxiv	Retrospective Cohort Study	Mar-20	China
Wan, S et al	Journal of Medical Virology	Retrospective Cohort Study	Mar-20	China
Zhang, Y et al	Liver International	Retrospective Cohort Study	Mar-20	China
Xu, Z et al	The Lancet	Case Report	Fab-20	China
Arentz et al	JAMA	Retrospective Cohort Study	Mar-20	USA
Hajifathalian et al	Gastroenterology	Retrospective Cohort Study	May-20	USA
Kujawski et al	MedRxiv	Retrospective Cohort Study	Mar-20	USA
Young et al	JAMA	Case series	Mar-20	Singapore
Sun et al	Clinical Infectious Diseases	retrospective case-control	Mar-20	Singapore
Pung et al	The Lancet	Retrospective Cohort Study	Mar-20	Singapore
Tabata et al	MedRxiv	Retrospective Cohort Study	Apr-20	Japan
Kluytmans et al	MedRxiv	cross-sectional study	Mar-20	Netherlands
Qian et al	Quarterly Journal of Medicine	Retrospective case series	Mar-20	China
Luo et al	Clinical Gastroenterology and Hepatology	Retrospective cohort study	Mar-20	China
Zhou F et al	Lancet	Retrospective Cohort Study	Mar-20	China
Chen T et al	BMJ	Retrospective Case Series	Mar-20	China
Xu H et al	MedRxiv	Retrospective Cohort Study	Mar-20	China
Shi S et al	JAMACardio	Retrospective Cohort Study	Mar-20	China
Han R et al	Lancet	Retrospective Cohort Study	Jun-20	China
Xu S et al	MedRxiv	Retrospective analysis	Mar-20	China
Ma L et al	MedRxiv	Retrospective Study	Mar-20	China
Liu L et al	Microbes and infection	Retrospective Study	May-20	China
Mao L et al	JAMANeurology	Case Series	Apr-20	China
Ai JW et al	Frontiers in Medicine	Cross sectional study	Jun-20	China
Liu Y et al	MedRxiv	Retrospective Study	May-20	China
Shu L et al	Lancet	Retrospective Cohort Study	Apr-20	China
Wei L et al	MedRxiv	Retrospective Cohort Study	May-20	China
Zhao Z et al	MedRxiv	Retrospective Study	Mar-20	China
Zhao W et al	MedRxiv	Retrospective Cohort Study	Mar-20	China
Yang P et al	MedRxiv	Retrospective Study	Mar-20	China
Li K et al	Investigative Radiology	Retrospective Study	Jun-20	China
Qi D et al	MedRxiv	Retrospective Descriptive study	Mar-20	China
Wen Y et al	MedRxiv	Retrospective Study	Mar-20	China
Xu Y et al	MedRxiv	Retrospective Observational Study	Mar-20	China
Yan S et al	MedRxiv	Retrospective Study	Mar-20	China
Wang L et al	European Respiratory Journal	Retrospective Study	Apr-20	China
Chen X et al	MedRxiv	Observational study	Mar-20	China
Liu S et al	BMC Infectious Diseases	Cohort Study	Jun-20	China

Study	Journal	Study type	Date	Country
Yao et al	Chinese Journal of Hepatology	Retrospective Study	Mar-20	China
Tian S et al	MedRxiv	Retrospective study	Mar-20	China
Lu H et al	MedRxiv	Descriptive Study	Feb-20	China
Fu H et al	MedRxiv	Observational Study	Mar-20	China
Fu H et al	MedRxiv	Observational Study	Mar-20	China
Chen D et al	MedRxiv	Retrospective Study	Feb-20	China
Kuang et al	Gastroenterology	Retrospective study	Feb-20	China
Rubin et al	Journal of Clinical And Translational Science	Cohort	May-20	USA
Covid-19 National Emergency Response Center South Korea	Osong Public Health andResearch Perspectives	Case Series	Feb-20	South Korea
Pung et al	Lancet	Retrospective	Mar-20	Singapore
Wolfel et al	Nature	Case series	Apr-20	Germany
Dreher et al	Dtsch Arztebl International	Retrospective	Apr-20	Germany
Gritti et al	MedRxiv	Observational Cohort Study	Apr-20	Italy
Spiteri et al	Euro Surveillance	Surveillance	Mar-20	Germany, Finland, Italy, Russia, Spain, France, Sweden, and Belgium
Covid-19 National Incident Room Surveillance Team Australia	Communicable Diseases Intelligence (2018)	Epidemiology Report	Mar-20	Australia
An P et. al.	European Respiratory Journal	Case series	Jan-20	China
Chan et. al.	MedRxiv	Case series	Jan-20	China
Chang et al	BMC Infectious Diseases	Case series	Jan-20	China
Chen et al	Chinese Journal of Hepatology	Case series	Jan-20	China
Cheung et al	MedRxiv	Case series	Feb-20	China
Fan H et al	MedRxiv	Case series	Feb-20	China
Fernandez-Ruiz et al	MedRxiv	Case series	Mar-20	Spain
Guan et al	MedRxiv	Retrospective cohort	Jan-20	China
Han et al	MedRxiv	Retrospective cohort	Feb-20	China
Hsih et al	Clinics and Research in Hepatology and Gastroenterology	Case series	Feb-20	Taiwan
Huang et al	Allergy (John Wiley and Sons Ltd.)	Case series	Feb-20	China
Huang et al	Indones J Intern Med	Case series	Feb-20	China
Kim ES et al	BMJ	Case series	Feb-20	Korea
Klopfenstein et al	Gastroenterology	Case series	Mar-20	France
Liu K et al	BMJ	Case series	Jan-20	China
Lechien et al	Gastroenterology	Case series	Feb-20	Europe
Liu Y et al	The American Journal of GASTROENTEROLOGY	Case series	Jan	China
Pan F et al	European Journal of Case Reports in Internal Medicine	Retrospective cohort	Feb-20	China
Redd et al	Gastroenterology	Retrospective cohort	Apr-20	US

Study	Journal	Study type	Date	Country
Ren et al	Digestive Diseases and Sciences (Springer)	Case series	Dec-19	China
Shi H et al	World Journal of Clinical Cases	Retrospective cohort	Jan-20	China
Song et al	British Journal of Surgery	Case series	Jan-20	China
Wan Y et al	Journal of travel medicine	Case series	Mar-20	China
Wang L (b) et. al.	Journal Of Medical Virology	Case series	Feb-20	China
Wang L (c) et. al.	Journal Of Medical Virology	Case series	Feb-20	China
Wang X et. al.	Journal of Medical Virology	Case series	Feb-20	China
Wang Z et. al.	The Lancet	Case series	Jan-20	China
Wei X-S et. al.	The Lancet	Case series	Feb-20	China
Wu J (a) et. al.	JAMA	Retrospective cohort	Feb-20	China
Wu J (b) et al	BMJ	Case series	20-Feb	China
Wu Y et. al.	MedRxiv	Case series	Mar-20	China
Xia X et. al.	MedRxiv	Case series	Mar-20	China
Xiao F et. al.	MedRxiv	Case series	Feb-20	China
Xie H et. al.	Journal of Medical Virology	Case series	Feb-20	China
Xiong Y et. al.	Liver International	Case series	Feb-20	China
Xu X et al	The Lancet	Case series	Feb-20	China
Yu P et. al.	JAMA	Case series	Jan-20	China
Zhang J (b) et. al	Gastroenterology	Case series	Feb-20	China
Zhao X-Y et. al.	MedRxiv	Case series	Feb-20	China
Zhou S et. al.	JAMA	Case series	Jan-20	China
Zou L et. al.	Clinical Infectious Diseases	Case series	Jan-20	China
Sulaiman et al.	JGH Open	retrospective descriptive study	Aug-20	Iraq
Elmunzer et al	Clinical Gastroenterology and Hepatology	observational cohort study	Sept-20	USA and Canada
Laszkowska et al	Clinical Gastroenterology and Hepatology	retrospective study	Sept-20	USA
Hundt et al	Hepatology	Retrospective cohort study	July-20	USA and Canada
Ferm et al	Clinical Gastroenterology and Hepatology	Retrospective cohort study	Sept-20	USA
Zhan et al	Journal of International Medical Research	retrospective study	July-20	China
Ramachandran et al	Digestive Diseases	Retrospective cohort study	June-20	USA
Suleyman et al	JAMA	Case series	June-20	USA
Khader et al	Radiology Case Reports	Case report	Nov-20	Qatar
Grande G et al	ACG Case Reports	Case Report	Sept-20	Italy
Gulen M	Clinics and Research in Hepatology and Gastroenterology	Case Report	Sep-20	Turkey
Cholankeril et al	The American Journal of GASTROENTEROLOGY	Retrospective study	Sept-20	USA
Cavaliere et al	Gastrointestinal endoscopy	Case series	Aug-20	China?
Hassani AH et al	Gastroenterology and Hepatology from Bed to Bench	Case reports	Sep-20	Iran

Study	Journal	Study type	Date	Country
Wu CY et al	Journal of International Medical Research	Case report	Sept-20	China
Wang K et al	Open Forum Infectious Disease	Case report	Sept-20	China
Dietrich CG et al	European Journal of Gasntroenterology and Hepatology	Case report	Nov-20	Germany
Kandasamy S et al	Annals of-Hepato-Biliary-Pancreatic Surgery	Case Report	Nov-20	India
Wagner J et al	SN comprehensive clinical medicine	Retrospective cohort study	Sep-20	USA
Wahab SF et al	BMJ Case Reports	Case Report	Aug-20	Denmark
Cheung S et al	American jounral of Case Reports	Case Report	Aug-20	USA
Docherty AB. et al.	Diseases	Retrospective cohort study	April-20	UK
Fanelli V. et al.	Critical Care	Retrospective cohort study	April-20	Spain
CDC USA	Morb. Mortal. Wkly Rep	Retrospective cohort study	April-20	USA
CDC USA	Morb. Mortal. Wkly Rep	Retrospective cohort study	April-20	USA
Borobia A. et al.	Journal of Clinical Medicine	Retrospective cohort study	June-20	Spain
Gil-Rodrigo A. et al	Emergencias	Retrospective cohort study	Aug-20	Spain
Livanos AE. et al.	MedRxiv	Retrospective cohort study	Nov-20	USA
Bannaga AS. et al	Clinical Medicine Journal	Retrospective cohort study	Sept-20	UK
Moura DTH et al	Clinics	Retrospective cohort study	July-20	Brazil
A. Papa et al	European Review for Medical and Pharmacological Sciences	case control	July-20	Italy
N Aumpan et al.	JGH Open	Retrospective cohort study	July-20	Thailand
Ping Lei et al	Hepatology international	Retrospective cohort study	Sept-20	China
Mo P, et al.	Clinical Infecious Disease	Retrospective cohort study	Sept-20	China
Tsibouris et al	Annals of Gastroenterology	Retrospective cohort study	June-20	Greece
Aghemo et al	Clinical Gastroenterology and Hepatology	Retrospective cohort study	Sept-20	Italy
Klopfenstein et al	Clinical Gastroenterology and Hepatology	Retrospective cohort study	June-20	France
Colaneri et al	Euro Surveillance	Retrospective cohort study	Apr-20	Italy

Table. 2 The Methodical Index for Non-randomized Studies (MINORS)

Study	Clearly stated aim	Inclusion of consecutive patients	Prospective data collection	Endpoints appropriate to study aim	Endpoints appropriate to study aim	Follow-up period appropriate to study aim	Adequate control group	Adequate statistical analyses	Total
Siegel et al	1	1	0	0	0	0	0	0	2
Pazgan-simon et al	1	0	0	1	0	0	0	0	2
Yang, X et al	1	0	0	1	0	0	0	0	2
Zhang, J et al	2	2	2	1	0	0	0	1	8
Azwar et al	1	1	0	1	0	1	0	0	4
Jin, X et al	2	2	2	2	0	1	1	1	11

Nobel et al	2	2	2	1	0	0	0	1	8
Lin et al	1	1	0	2	0	1	0	1	6
Zhou et al	2	2	0	2	0	0	0	1	7
Pan et al	2	2	1	0	0	0	0	1	6
Poggiali et al	2	0	0	1	0	1	0	2	6
Cholankeril et al	2	1	2	0	2	0	0	1	8
Fu et al	2	0	1	1	0	0	0	0	4
Li et al	2	0	2	0	0	0	0	0	4
Saeed et al	2	1	2	1	0	0	0	1	7
Arashiro et al.	2	0	0	2	0	0	0	1	5
Yang F et al	2	1	2	0	2	0	0	1	8
Guillen, E et al	2	1	1	1	0	1	0	2	8
Chen, Y et al	1	1	0	2	0	1	0	1	6
Chen Q et al	2	1	0	1	0	0	0	1	5
Huang et al	2	2	1	0	0	0	0	1	6
Chen, N et al	2	0	1	1	0	0	0	2	6
Wang et al	2	0	2	0	0	0	0	2	6
Xu, X et al	2	1	0	1	0	0	0	2	6
Fan et al	2	0	1	1	0	0	0	2	6
Zhang, B et al	2	1	2	0	0	0	0	2	7
Huang Y et al	2	0	1	1	0	0	0	2	6
Wan, S et al	2	0	2	0	0	0	0	2	6
Zhang, Y et al	2	1	0	1	0	0	0	2	6
Xu, Z et al	2	0	0	0	0	0	0	2	4
Arentz et al	1	2	2	2	0	0	0	1	8
Hajifathalian et al	2	1	1	1	0	0	0	2	7
Kujawski et al	2	1	1	1	0	0	0	1	6
Young et al	2	1	0	1	0	0	0	2	6
Sun et al	2	0	0	0	0	0	0	2	4
Pung et al	2	1	2	1	0	0	0	1	7
Tabata et al	2	2	0	1	0	0	0	1	6
Kluytmans et al	2	1	1	0	0	0	0	1	5
Qian et al	2	0	0	1	0	1	0	2	6
Luo et al	0	1	1	1	2	3	0	1	9
Zhou F et al	1	0	1	2	0	2	0	2	6
Chen T	1	1	1	2	1	0	0	2	8
Xu H et al	2	1	0	3	0	0	0	1	7
Shi S et al	2	1	1	0	0	0	0	2	6
Han R et al	1	0	0	0	0	1	0	2	4
Xu S et al	0	1	1	1	2	3	0	1	9

Study	Clearly stated aim	Inclusion of consecutive patients	Prospective data collection	Endpoints appropriate to study aim	Endpoints appropriate to study aim	Follow-up period appropriate to study aim	Adequate control group	Adequate statistical analyses	Total
Ma L et al	2	0	1	3	0	3	0	1	9
Liu L et al	2	0	2	0	0	0	0	2	6
Mao L et al	2	1	0	1	0	0	0	2	6
Ai JW et al	c	0	0	0	0	0	0	2	4
Shu L et al	1	0	2	0	0	0	0	1	4
Wei L et al	2	1	1	1	0	0	0	2	7
Zhao Z et al	1	1	0	1	0	0	0	1	4
Zhao W et al	2	0	2	0	0	0	0	2	6
Yang P et al	2	1	0	1	0	0	0	2	6
Li K et al	2	0	0	0	0	0	0	2	4
Qi D et al	2	1	0	1	0	0	0	1	5
Wen Y et al	2	1	1	0	0	0	0	1	5
Xu Y et al	1	0	0	0	0	1	0	2	4
Yan S et al	0	1	1	1	2	3	0	1	9
Wang L et al	2	0	1	3	0	4	0	2	11
Chen X et al	2	1	0	3	0	0	0	1	7
Liu S et al	2	1	1	0	0	0	0	2	6
Fan L et al	1	0	1	0	0	1	0	2	5
Yao et al	0	1	1	1	2	3	0	1	9
Tian S et al	2	0	1	3	0	4	0	1	10
Lu H et al	2	1	0	1	0	0	0	2	6
Fu H et al	2	1	1	0	0	0	0	1	5
Fu H et al	2	1	0	3	0	0	0	1	7
Chen D et al	2	1	1	0	0	0	0	2	6
Kuang et al	1	0	0	0	0	1	0	2	4
Rubin et al	0	1	1	1	2	3	0	1	9
COVID-19 National Emergency Response Center	2	0	1	3	0	4	0	2	12
Pung et al	2	2	0	1	0	0	0	1	6
Wolfel	2	1	0	1	0	0	0	1	5
Dreher et al	2	1	1	0	0	0	0	1	5
Gritti et al	2	0	0	1	0	1	0	2	6
Spiteri et al	0	1	1	1	2	3	0	1	9

Study	**Clearly stated aim**	**Inclusion of consecutive patients**	**Prospective data collection**	**Endpoints appropriate to study aim**	**Endpoints appropriate to study aim**	**Follow-up period appropriate to study aim**	**Adequate control group**	**Adequate statistical analyses**	**Total**
Covid-19 National Incident Surveillance	2	0	1	4	0	4	0	2	13
An P et. al.	1	1	1	2	1	0	0	2	8
Chan F-W et.al.	2	1	0	3	0	0	0	1	7
Chang D et. al.	2	1	1	0	0	0	0	2	6
Chen Q (b) et. al.	1	0	0	0	0	1	0	2	4
Cheung K et. al.	0	1	1	1	2	3	0	1	9
Fan H et. al.	2	0	1	3	0	3	0	1	9
FernandezRuiz et. al.	2	0	2	0	0	0	0	2	6
Guan W-j et. al.	2	1	0	1	0	0	0	2	6
Han C et. al.	1	0	0	0	0	0	0	2	4
Hsih W-H et. al.	1	0	2	0	0	0	0	1	4
Huang R et. al.	2	1	1	1	0	0	0	2	7
Huang WH et. al.	1	1	0	1	0	0	0	1	4
Kim ES et. al.	2	0	2	0	0	0	0	2	6
Klopfenstein T et. al.	2	1	0	1	0	0	0	2	6
Liu K et. al.	2	0	0	0	0	0	0	2	4
Lechien J et. al.	2	1	0	1	0	0	0	1	5
Liu Y et. al.	2	1	1	0	0	0	0	1	5
Pan F et. al.	1	0	0	0	0	1	0	2	4
Redd W et. al.	0	1	1	1	2	3	0	1	9
Ren L et. al.	2	0	1	3	0	4	0	2	11
Shi H et. al.	2	1	0	3	0	0	0	1	7
Song F et. al.	2	1	1	0	0	0	0	2	6
Wan Y et. al.	1	0	1	0	0	1	0	2	5
Wang L (b) et.	0	1	1	1	2	3	0	1	9
Wang L (c) et. al.	2	0	1	3	0	4	0	1	10
Wang X et. al.	2	1	0	1	0	0	0	2	6
Wang Z et. al.	2	1	1	0	0	0	0	1	5
Wei X-S et. al.	2	1	0	3	0	0	0	1	7
Wu J (a) et. al.	2	1	1	0	0	0	0	2	6
Wu J (b) et al	1	0	0	0	0	1	0	2	4
Wu Y et. al.	0	1	1	1	2	3	0	1	9
Xia X et. al.	2	0	1	3	0	4	0	2	12
Xiao F et. al.	2	2	0	1	0	0	0	1	6

Xie H et. al.	1	0	0	0	0	1	0	2	4
Xiong Y et. al.	2	1	0	3	0	0	0	1	7
Xu X et al	2	1	1	0	0	0	0	2	6
Yu P et. al.	1	0	0	0	0	1	0	2	4
Zhang J (b) et. al.	0	1	1	1	2	3	0	1	9
Zhao X-Y et. al.	2	0	1	3	0	4	0	1	10
Zhou S et. al.	2	1	0	1	0	0	0	1	5
Zou L et. al.	2	1	1	0	0	0	0	1	5
Sulaiman et al.	1	0	0	0	0	1	0	2	4
Elmunzer et al	0	1	1	1	2	3	0	1	9
Laszkowska et al	2	0	1	3	0	4	0	2	11
Hundt et al	2	1	0	3	0	0	0	1	7
Ferm et al	2	1	1	0	0	0	0	2	6
Zhan et al	1	0	1	0	0	1	0	2	5
Ramachandran et al	0	1	1	1	2	3	0	1	9
Suleyman et al	2	0	1	3	0	4	0	1	10
Docherty AB. et al.	2	1	0	1	0	0	0	2	6
Fanelli V. et al.	2	1	2	0	0	0	0	1	6
CDC USA	2	1	0	3	0	0	0	1	7
CDC USA	2	1	1	0	0	0	0	2	6
Borobia A. et al.	2	2	1	0	0	1	0	2	8
Gil-Rodrigo et al	0	1	1	1	2	3	0	1	9
Khader et al	2	0	1	3	0	4	0	2	12
Grande G et al	2	2	0	1	0	0	0	1	6
Gulen et al	2	2	0	1	0	1	0	2	8
Cholankeril et al	2	1	0	3	0	0	0	1	7
Cavaliere K et al	2	1	1	0	0	0	0	2	6
Hassani AH et al	1	1	1	0	0	1	0	2	6
Wu CY et al	2	1	0	3	0	0	0	1	7
Wang K et al	2	1	1	0	0	0	0	2	6
Dietrich al	1	0	1	0	0	1	0	2	5
Kandasamy et al	0	1	1	1	2	3	0	1	9
Wagner J et al	2	0	1	3	0	4	0	1	10
Wahab SF	2	1	0	1	0	0	0	2	6
Cheung S et al	2	1	1	0	0	0	0	1	5
Livanos et al	2	1	0	3	0	0	0	1	7
Bannaga et al	2	1	1	0	0	0	0	2	6
Moura et al	1	2	0	0	0	1	0	2	6
A. Papa et al	2	1	0	3	0	0	0	1	7
N Aumpan et al.	2	0	1	3	0	4	0	1	10
Ping Lei et al	2	1	0	1	0	0	0	2	6

Mo P, et al.	2	2	2	0	0	0	0	1	7
Tsibouris et al	2	1	0	3	0	0	0	1	7
Klopfenstein et al	2	1	1	0	0	0	0	2	6
Aghemo et al	1	2	2	0	0	1	0	2	8
Colaneri et al	0	1	1	1	2	3	0	1	9

Table. 3 Gastrointestinal symptoms reported by each study

Study	Total number of patients in each study (n)	Abdominal pain (n)	Diarrhea (n)	Nausea (n)	Vomiting (n)	Anorexia or loss of appetite (n)	Loss of taste (n)	Elevated liver enzymes (n)
Siegel et al	3	3	3	2	2	0	0	0
Pazgan-simon et al	1	1	0	1	0	1	0	0
Yang, X et al	1	1	0	0	0	0	0	0
Zhang, J et al	140	8	18	24	7	17	0	8
Azwar et al	1	1	0	0	1	0	0	0
Jin, X et al	651	0	56	13	14	0	0	64
Nobel et al	278	0	56	63	63	0	0	0
Lin et al	95	2	23	17	4	17	0	31
Zhou et al	254	3	46	21	15	0	0	0
Pan et al	204	2	35	0	4	81	0	0
Poggiali et al	10	1	6		3	0	0	0
Cholankeril et al	116	10	12	1	1	22	0	26
Fu et al	1	0	0	0	1	0	0	0
Li et al	1	0	1	0	0	1	0	0
Saeed et al	9	9	1	8	5	0	0	0
Arashiro et al.	1	0	1	1	0	1	0	0
Yang F et al	92	0	0	0	0	0	0	15
Guillen, E et al	1	0	0	0	1	0	0	0
Chen, Y et al	42	5	7	4	3	0	0	0
Chen Q et al	9	0	2	0	0	0	0	0
Huang C et al	41	0	1	0	0	0	0	0
Chen, N et al	99	0	2	1	1	0	0	63
Wang et al	138	3	14	14	5	55	0	
Xu, X et al	62	0	3	0	0	0	0	0
Fan et al	148	0	6	6	0	0	0	75
Zhang, B et al	82	0	10	0	2	0	0	0
Huang Y et al	36	0	3	0	0	0	0	22
Wan, S et al	135	0	18	4	0	6	0	0

Study	Total number of patients in each study (n)	Abdominal pain (n)	Diarrhea (n)	Nausea (n)	Vomiting (n)	Anorexia or loss of appetite (n)	Loss of taste (n)	Elevated liver enzymes (n)
Zhang, Y et al	115	0	0	0	0	0	0	28
Xu, Z et al	1	0	0	0	0	0	0	1
Arentz et al	21	0	0	0	0	0	0	8
Hajifathalian et al	1059	72	234	168	91	240	57	656
Kujawski et al	12	1	1	0	0	0	0	0
Young et al	18	0	3	0	0	0	0	0
Sun et al	54	0	0	0	0	0	0	0
Pung et al	36	0	4	1	0	0	0	0
Tabata et al	104	0	18	0	0	0	0	9
Kluytmans et al	86	5	16	0	0	15	6	0
Qian et al	91	0	21	11	6	23	0	0
Luo et al	183	45	68	134	119	-	-	183
Zhou F et al	191	-	9	7	7	-	-	59
Chen T	274	19	77	24	16	-	-	84
Xu H et al	1324	-	28	-	-	55	-	-
Shi S et al	416	-	29	-	-	-	-	416
Han R et al	108	-	15		-	-	-	-
Xu S et al	355	-	130	-	-	-	-	102
Ma L et al	81	-	6	-	-	-	-	31
Liu L et al	153	1	14	2	3	-	-	-
Mao L et al	214	10	41	-	-	-	-	26
Ai JW et al	102	4	15	9	2	-	-	26
Shu L et al	545	-	49	0	0	-	-	41
Wei L et al	100	-	2	-	2	-	-	17
Zhao Z et al	75	1	7	-	-	-	-	15
Zhao W et al	77	-	1	6		-	-	26
Yang P et al	55	-	2	-	-	-	-	-
Li K et al	83	-	7	-	-	-	-	-
Qi D et al	267	-	10	6	-	46	-	20
Wen Y et al	417	-	29	-	-	-	-	-
Xu Y et al	45	-	0	-	-	-	-	17
Yan S et al	168	7	12	9	7	-	-	18
Wang L et al	18	-	3	-	-	-	-	4
Chen X et al	291	1	25	17	-	-	-	44
Liu S et al	620	-	53	-	-	-	-	420
Fan L et al	55	-	6	-	4	-	-	
Yao et al	40	-	3	3	-	-	-	21

Study	Total number of patients in each study (n)	Abdominal pain (n)	Diarrhea (n)	Nausea (n)	Vomiting (n)	Anorexia or loss of appetite (n)	Loss of taste (n)	Elevated liver enzymes (n)
Tian S et al	37	-	8	-	-	-	-	4
Lu H et al	265	-	17	6	-	-	-	-
Fu H et al	52	-	7	1	-	-	-	-
Fu H et al	36	-	3	-	-	-	-	4
Chen D et al	175	-	35	-	-	-	-	-
Kuang et al	944	-	21	-	-	-	-	-
Rubin et al	54	-	-	-	-	-	-	-
COVID-19 National Emergency Response Center	28	1	2	-	-	-	-	-
Pung et al	17	-	4	1	-	-	-	-
Wolfel	9	-	2	-	-	-	-	-
Dreher et al	50	-	8	1	2	-	-	-
Gritti et al	21	-	5	-	-	-	-	-
Spiteri et al	38	-	1	1	-	-	-	-
Covid-19 National Incident Room Surveillance Team Australia	295	6	48	34	-	-	-	-
An P et. al.	9	-	1	1	1	6	-	-
Chan F-W et.al.	6	-	2	-	-	-	-	-
Chang D et. al.	13	-	1	-	-	-	-	-
Chen Q (b) et. al.	145	-	39	24	6	-	-	-
Cheung K et. al.	59	7	13	-	1	-	-	-
Fan H et. al.	101	-	2	7		-	-	-
FernandezRuiz et. al.	17	1	3	-	-	-	-	-
Guan W-j et. al.	1099	-	42	55	55	-	-	-
Han C et. al.	206	9	67	-	24	32	-	-
Hsih W-H et. al.	2	1	1	-	-	-	-	-
Huang R et. al.	11	-	1	-	-	-	-	-
Huang WH et. al.	2	-	-	-	-	2	-	-
Kim ES et. al.	28	1	3	-	-	-	-	-
Klopfenstein T et. al.	114	19	55	25	9	-	-	-

Study	Total number of patients in each study (n)	Abdominal pain (n)	Diarrhea (n)	Nausea (n)	Vomiting (n)	Anorexia or loss of appetite (n)	Loss of taste (n)	Elevated liver enzymes (n)
Liu K et. al.	137	-	11	-	-	-	-	-
Lechien J et. al.	417	125	208	91	91	-	-	-
Liu Y et. al.	12	-	2	2		-	-	-
Pan F et. al.	21	-	-	-	-	9	-	-
Redd W et. al.	318	46	107	84	49	110	-	-
Ren L et. al.	5	-	0	-	-	-	-	-
Shi H et. al.	81	-	3	-	4	-	-	-
Song F et. al.	51	-	5	3	-	9	-	-
Wan Y et. al.	230	-	49	-	-	-	-	-
Wang L (b) et.	26	-	0	-	-	-	-	-
Wang L (c) et. al.	339	-	43	13	-	94	-	-
Wang X et. al.	1021	37	152	-	36	-	-	-
Wang Z et. al.	4	-	0	-	-	-	-	-
Wei X-S et. al.	84	2	26	16	6	-	-	-
Wu J (a) et. al.	80	-	1	1	1	-	-	-
Wu J (b) et al	80	-	7	-	-	-	-	-
Wu Y et. al.	74	-	26	-	-	-	-	-
Xia X et. al.	10	-	1	1	-	-	-	-
Xiao F et. al.	73	-	26	-	-	-	-	-
Xie H et. al.	79	-	7	-	-	-	-	-
Xiong Y et. al.	42	-	10	-	-	-	-	-
Xu X et al	90	-	5	5	2	-	-	-
Yu P et. al.	4	-	-	-	-	4	-	-
Zhang J (b) et. al.	14	-	0	-	0	-	-	-
Zhao X-Y et. al.	91	2	13	10	-	10	-	-
Zhou S et. al.	62	9	9	-	-	-	-	-
Zou L et. al.	18	-	1	1	-	1	-	-
Sulaiman et al.	140	42	41	-	32	40		
Elmunzer et al	1052	-	357	284	168	115	-	554
Laszkowska et al	1084	334	657	649	-	-	-	-
Hundt et al	1827	-	-	-	-	-	-	1158
Ferm et al	892	70	177	148	91	70	21	-
Zhan et al	405	41	112	-	76	170	-	-
Ramachandran et al	150	3	15	6	6	-	-	-
Suleyman et al	463	-	100	94	53	11	-	-
Docherty AB. et al.	16,749	1146	2292	2178	-	-	-	-

Study	Total number of patients in each study (n)	Abdominal pain (n)	Diarrhea (n)	Nausea (n)	Vomiting (n)	Anorexia or loss of appetite (n)	Loss of taste (n)	Elevated liver enzymes (n)
Fanelli V. et al.	14,688	-	881	-	-	6	-	-
CDC USA	10,994	1329	3353	1746	-	-	-	-
CDC USA	6760	-	1507	923	-	-	-	-
Borobia A. et al.	2226	-	484	299	-	-	-	-
Gil-Rodrigo et al	1000	66	186	75	-	-	-	-
Khader et al	1	1	-	1	-	-	-	-
Grande G et al	1	-	-	-	1	-	-	-
Gulen et al	1	1	1	-	-	-	-	-
Cholankeril et al	207	-	22	22	22	-	-	-
Cavaliere K et al	6	-	-	-	2	-	-	-
Hassani AH et al	2	2	-	-	-	-	-	-
Wu CY et al	1	1	-	1	-	-	-	-
Wang K et al	2	2	-	-	-	-	-	-
Dietrich al	1	1	-	1	-	-	-	-
Kandasamy et al	1	1	-	1	1	-	-	-
Wagner J et al	99							
Wahab SF	1	1	1	-	-	-	-	-
Cheung S et al	1	1	-	1	1	-	-	-
Livanos et al	634	-	245	157	-	-	-	-
Bannaga et al	321	15	13	15	-	-	-	-
Moura et al	400	24	69	55	30	46	-	-
A. Papa et al	34	1	1	1	-	-	-	-
N Aumpan et al.	40	2	6	2	2	7	-	-
Ping Lei et al	115	-	14	9	9	9	-	-
Mo P, et al.	155	-	7	3	3	-	-	55
Tsibouris et al	61	2	11	2	2	-	-	-
Klopfenstein et al	114	19	55	25	9	-	-	-
Aghemo et al	325	-	69	-	11	-	-	54
Colaneri et al	44	-	3	-	-	-	-	-
Total	78798	3586	13044	7645	1195	1331	84	4405

Table. 4 Newcastle-Ottawa Scale scores to assess the quality of the studies (for cohort and case control studies)

	Selection			Comparability	Outcome			
Study	**Representativeness of sample (maximum: one star)**	**Sample size (maximum: one star)**	**Assessment of the exposure (maximum: one star)**	**Comparability of cohorts on the basis of the design or analysis (maximum: 2 stars)**	**Assessment of the outcome (maximum: one star)**	**Was follow up long enough? (maximum: one star)**	**Adequacy of follow up cohorts (maximum: one star)**	**Total score (maximum: 8 stars)**
Siegel et al			*					* (1)
Pazgan-simon et al			*					* (1)
Yang, X et al								* (1)
Zhang, J et al	*		*	*	*		*	***** (5)
Azwar et al			*					* (1)
Jin, X et al	*		*	*		*		**** (4)
Nobel et al			*		*			** (2)
Lin et al	*	*	*	*	*	*	*	******* (7)
Zhou et al	*			*	*		*	**** (4)
Pan et al	*	*	*	**	*	*		******* (7)
Poggiali et al	*		*		*			*** (3)
Cholankeril et al	*	*	*	*	*		*	****** (6)
Fu et al			*					* (1)
Li et al			*					* (1)
Saeed et al	*			*		*	*	**** (4)
Arashiro et al.								
Yang F et al	*		*	*	*		*	******(5)
Guillen, E et al			*					* (1)
Chen, Y et al	*	*	*	*	*		*	****** (6)
Chen Q et al			*					* (1)
Huang C et al	*		*	*	*		*	***** (5)
Chen, N et al	*	*		*			*	**** (4)

	Selection			Comparability	Outcome			
Study	**Representativeness of sample (maximum: one star)**	**Sample size (maximum: one star)**	**Assessment of the exposure (maximum: one star)**	**Comparability of cohorts on the basis of the design or analysis (maximum: 2 stars)**	**Assessment of the outcome (maximum: one star)**	**Was follow up long enough? (maximum: one star)**	**Adequacy of follow up cohorts (maximum: one star)**	**Total score (maximum: 8 stars)**
Wang et al			*		*			** (2)
Xu, X et al	*	*	*	*	*		*	****** (6)
Fan et al	*			*	*		*	**** (4)
Zhang, B et al	*		*	*	*		*	***** (5)
Huang Y et al	*			*	*		*	***** (4)
Wan, S et al	*	*		*		*	*	***** (5)
Zhang, Y et al	*	*		*	*	*	*	****** (6)
Xu, Z et al			*					* (1)
Arentz et al	*			*		*	*	**** (4)
Hajifathalian et al	*	*		*	*		*	***** (5)
Kujawski et al	*	*		*			*	**** (4)
Young et al			*					* (1)
Sun et al			*		*			** (2)
Pung et al	*	*	*	*	*		*	****** (6)
Tabata et al	*			*	*		*	**** (4)
Kluytmans et al			*					* (1)
Qian et al			*		*			** (2)
Luo et al			*					* (1)
Zhou F et al			*		*			** (2)
Chen T			*		*			** (2)

	Selection			Comparability	Outcome			
Study	**Representativeness of sample (maximum: one star)**	**Sample size (maximum: one star)**	**Assessment of the exposure (maximum: one star)**	**Comparability of cohorts on the basis of the design or analysis (maximum: 2 stars)**	**Assessment of the outcome (maximum: one star)**	**Was follow up long enough? (maximum: one star)**	**Adequacy of follow up cohorts (maximum: one star)**	**Total score (maximum: 8 stars)**
Xu H et al			*					* (1)
Shi S et al			*					* (1)
Han R et al			*		*			** (2)
Xu S et al			*		*			** (2)
Ma L et al			*					* (1)
Liu L et al			*		*			** (2)
Mao L et al			*		*			** (2)
Ai JW et al			*					* (1)
Shu L et al			*					* (1)
Wei L et al			*		*			** (2)
Zhao Z et al			*					* (1)
Zhao W et al			*		*			** (2)
Yang P et al			*		*			** (2)
Li K et al			*		*			** (2)
Qi D et al			*		*			** (2)
Wen Y et al			*		*			** (2)
Xu Y et al			*		*			** (2)
Yan S et al			*		*			** (2)

	Selection			Comparability	Outcome			
Study	Representativeness of sample (maximum: one star)	Sample size (maximum: one star)	Assessment of the exposure (maximum: one star)	Comparability of cohorts on the basis of the design or analysis (maximum: 2 stars)	Assessment of the outcome (maximum: one star)	Was follow up long enough? (maximum: one star)	Adequacy of follow up cohorts (maximum: one star)	Total score (maximum: 8 stars)
Wang L et al			*		*			** (2)
Chen X et al			*		*			** (2)
Liu S et al			*		*			** (2)
Fan L et al			*		*			** (2)
Yao et al			*		*			** (2)
Tian S et al			*		*			** (2)
Lu H et al			*		*			** (2)
Fu H et al			*		*			** (2)
Fu H et al			*		*			** (2)
Chen D et al		*	*		*			*** (3)
Kuang et al			*					* (1)
Rubin et al			*		*			** (2)
COVID-19 National Emergency Response Center			*		*			** (2)
Pung et al			*		*			** (2)
Wolfel			*		*			** (2)
Dreher et al			*		*			** (2)
Gritti et al			*		*			** (2)
Spiteri et al		*	*		*			*** (3)
Covid-19 National Incident Room Surveillance Team Australia			*					* (1)
An P et. al.			*					* (1)
Chan F-W et.al.			*		*			** (2)
Chang D et. al.			*		*			** (2)

	Selection			Comparability	Outcome			
Study	**Representativeness of sample (maximum: one star)**	**Sample size (maximum: one star)**	**Assessment of the exposure (maximum: one star)**	**Comparability of cohorts on the basis of the design or analysis (maximum: 2 stars)**	**Assessment of the outcome (maximum: one star)**	**Was follow up long enough? (maximum: one star)**	**Adequacy of follow up cohorts (maximum: one star)**	**Total score (maximum: 8 stars)**
Chen Q (b) et. al.			*					* (1)
Cheung K et. al.			*		*			** (2)
Fan H et. al.			*		*			** (2)
FernandezRuiz et. al.			*					* (1)
Guan W-j et. al.			*		*			** (2)
Han C et. al.		*	*		*			*** (3)
Hsih W-H et. al.			*		*			** (2)
Huang R et. al.			*		*			** (2)
Huang WH et. al.			*		*			** (2)
Kim ES et. al.			*		*			** (2)
Klopfenstein T et. al.			*		*			** (2)
Liu K et. al.			*		*			** (2)
Lechien J et. al.			*		*			** (2)
Liu Y et. al.			*		*			** (2)
Pan F et. al.		*	*		*			*** (3)
Redd W et. al.		*	*		*			*** (3)
Ren L et. al.			*		*			** (2)
Shi H et. al.			*		*			** (2)
Song F et. al.			*					* (1)
Wan Y et. al.			*		*			** (2)
Wang L (b) et.			*		*			** (2)
Wang L (c) et. al.			*		*			** (2)
Wang X et. al.			*					* (1)
Wang Z et. al.			*		*			** (2)
Wei X-S et. al.			*		*			** (2)
Wu J (a) et. al.		*	*		*			*** (3)
Wu J (b) et al			*		*			** (2)
Wu Y et. al.			*					* (1)
Xia X et. al.			*					* (1)
Xiao F et. al.			*					* (1)

	Selection			Comparability	Outcome			
Study	**Representativeness of sample (maximum: one star)**	**Sample size (maximum: one star)**	**Assessment of the exposure (maximum: one star)**	**Comparability of cohorts on the basis of the design or analysis (maximum: 2 stars)**	**Assessment of the outcome (maximum: one star)**	**Was follow up long enough? (maximum: one star)**	**Adequacy of follow up cohorts (maximum: one star)**	**Total score (maximum: 8 stars)**
Xie H et. al.			*		*			** (2)
Xiong Y et. al.			*		*			** (2)
Xu X et al			*		*			** (2)
Yu P et. al.			*					* (1)
Zhang J (b) et. al.			*					* (1)
Zhao X-Y et. al.			*		*			** (2)
Zhou S et. al.			*					* (1)
Zou L et. al.			*		*			** (2)
Sulaiman et al.			*		*			** (2)
Elmunzer et al			*		*			** (2)
Laszkowska et al			*		*			** (2)
Hundt et al			*		*			** (2)
Ferm et al			*		*			** (2)
Zhan et al			*		*			** (2)
Ramachandran et al			*		*			** (2)
Suleyman et al			*		*			** (2)
Docherty AB. et al.	*		*	*	*		*	***** (5)
Fanelli V. et al.	*			*	*		*	***** (4)
CDC USA	*		*	*	*		*	***** (5)
CDC USA	*	*	*	*	*		*	****** (6)
Borobia A. et al.	*	*	*	**	*		*	******* (7)
Gil-Rodrigo et al	*			*	*		*	***** (4)
Khader et al	*	*	*	*	*		*	****** (6)
Grande G et al	*	*	*	*		*	*	****** (6)
Gulen et al	*		*	*	*		*	***** (5)
Cholankeril et al	*			*	*		*	***** (4)

	Selection			Comparability	Outcome			
Study	**Representativeness of sample (maximum: one star)**	**Sample size (maximum: one star)**	**Assessment of the exposure (maximum: one star)**	**Comparability of cohorts on the basis of the design or analysis (maximum: 2 stars)**	**Assessment of the outcome (maximum: one star)**	**Was follow up long enough? (maximum: one star)**	**Adequacy of follow up cohorts (maximum: one star)**	**Total score (maximum: 8 stars)**
Cavaliere K et al	*	*	*	*	*		*	****** (6)
Hassani AH et al	*	*	*	*	*	*	*	******* (7)
Wu CY et al	*		*	*	*		*	***** (5)
Wang K et al	*			*	*		*	***** (4)
Dietrich al	*	*		*		*	*	***** (5)
Kandasamy et al	*			*	*		*	***** (4)
Wagner J et al	*		*	*	*		*	***** (5)
Wahab SF	*	*	*	*		*	*	****** (6)
Cheung S et al	c			*	*		*	***** (4)
Livanos et al	*		*	*	*		*	***** (5)
Bannaga et al	*			*	*		*	***** (4)
Moura et al	*	*		*		*	*	***** (5)
A. Papa et al	*	*		*	*	*	*	****** (6)
N Aumpan et al.	*		*	*	*		*	***** (5)
Ping Lei et al	*	*		*	*	*	*	****** (6)
Mo P, et al.	*			*	*		*	***** (4)
Tsibouris et al	*	*		*	*	*	*	****** (6)
Klopfenstein et al	*			*	*		*	***** (4)
Aghemo et al	*	*		*		*	*	***** (5)
Colaneri et al	*			*	*		*	***** (4)

Table. 5 Studies included in the Sensitivity Analysis

Study	Study type	Total No. of patients	Abdominal pain (n)	Diarrhea (n)	Nausea (n)	Vomiting (n)	Anorexia or loss of appetite (n)	Loss of taste (n)	Elevated liver enzymes (n)
Zhang, J et al	Retrospective cohort study	140	8	18	24	7	17		8
Jin, X et al	Retrospective cohort study	651	0	56	13	14	0	0	64
Lin et al	Retrospective cohort study	95	2	23	17	4	17	0	31
Zhou et al	Retrospective cohort study	254	3	46	21	15	0	0	0
Pan et al	Cross-sectional study	204	2	35	0	4	81	0	0
Cholankeril et al	Retrospective cohort study	116	10	12	1	1	22	0	26
Saeed et al	Retrospective cohort study	9	9	1	8	5	0	0	0
Yang F et al	Retrospective Cohort Study	92	0	0	0	0	0	0	15
Chen, Y et al	Retrospective Cohort Study	42	5	7	4	3	0	0	0
Huang, C et al	Prospective Cohort study	41	0	1	0	0	0	0	0
Chen, N et al	Retrospective Cohort Study	99	0	2	1	1	0	0	63

Study	Study type	Total No. of patients	Abdominal pain (n)	Diarrhea (n)	Nausea (n)	Vomiting (n)	Anorexia or loss of appetite (n)	Loss of taste (n)	Elevated liver enzymes (n)
Xu, X et al	retrospective case series	62	0	3	0	0	0	0	0
Fan et al	Retrospective Cohort Study	148	0	6	6	0	0	0	75
Zhang, B et al	Retrospective Cohort Study	82	0	10	0	2	0	0	0
Huang Y et al	Retrospective Cohort Study	36	0	3	0	0	0	0	22
Wan, S et al	Retrospective Cohort Study	135	0	18	4	0	6	0	0
Zhang, Y et al	Retrospective Cohort Study	115	0	0	0	0	0	0	28
Arentz et al	Retrospective Cohort Study	21	0	0	0	0	0	0	8
Hajifathalian et al	Retrospective Cohort Study	1059	72	234	168	91	240	57	656
Kujawski et al	Retrospective Cohort Study	12	1	1	0	0	0	0	0
Pung et al	Retrospective Cohort Study	36	0	4	1	0	0	0	0
Tabata et al	Retrospective Cohort Study	104	0	18	0	0	0	0	9

Study	Study type	Total No. of patients	Abdominal pain (n)	Diarrhea (n)	Nausea (n)	Vomiting (n)	Anorexia or loss of appetite (n)	Loss of taste (n)	Elevated liver enzymes (n)
Docherty AB. et al.	Retrospective Cohort Study	16,749	1146	2292	2178	-	-	-	-
Fanelli V. et al.	Retrospective Cohort Study	14,688	-	881	-	-	6	-	-
CDC USA	Retrospective Cohort Study	10,994	1329	3353	1746	-	-	-	-
CDC USA	Retrospective Cohort Study	6760	-	1507	923	-	-	-	-
Borobia A. et al.	Retrospective Cohort Study	2226	-	484	299	-	-	-	-
Gil-Rodrigo et al	Retrospective Cohort Study	1000	66	186	75	-	-	-	-
Khader et al	Retrospective Cohort Study	1	1	-	1	-	-	-	-
Grande G et al	Retrospective Cohort Study	1	-	-	-	1	-	-	-
Gulen et al	Retrospective Cohort Study	1	1	1	-	-	-	-	-
Cholankeril et al	Retrospective Cohort Study	207	-	22	22	22	-	-	-
Cavaliere K et al	Retrospective Cohort Study	6	-	-	-	2	-	-	-

Study	Study type	Total No. of patients	Abdominal pain (n)	Diarrhea (n)	Nausea (n)	Vomiting (n)	Anorexia or loss of appetite (n)	Loss of taste (n)	Elevated liver enzymes (n)
Hassani AH et al	Retrospective Cohort Study	2	2	-	-	-	-	-	-
Wu CY et al	Retrospective Cohort Study	1	1	-	1	-	-	-	-
Wang K et al	Retrospective Cohort Study	2	2	-	-	-	-	-	-
Dietrich al	Retrospective Cohort Study	1	1	-	1	-	-	-	-
Kandasamy et al	Retrospective Cohort Study	1	1	-	1	1	-	-	-
Wagner J et al	Retrospective Cohort Study	99							
Wahab SF	Retrospective Cohort Study	1	1	1	-	-	-	-	-
Cheung S et al	Retrospective Cohort Study	1	1	-	1	1	-	-	-
Livanos et al	Retrospective Cohort Study	634	-	245	157	-	-	-	-
Bannaga et al	Retrospective Cohort Study	321	15	13	15	-	-	-	-
Moura et al	Retrospective Cohort Study	400	24	69	55	30	46	-	-

Study	Study type	Total No. of patients	Abdominal pain (n)	Diarrhea (n)	Nausea (n)	Vomiting (n)	Anorexia or loss of appetite (n)	Loss of taste (n)	Elevated liver enzymes (n)
A. Papa et al	Retrospective Cohort Study	34	1	1	1	-	-	-	-
N Aumpan et al.	Retrospective Cohort Study	40	2	6	2	2	7	-	-
Ping Lei et al	Retrospective Cohort Study	115	-	14	9	9	9	-	-
Mo P, et al.	Retrospective Cohort Study	155	-	7	3	3	-	-	55
Tsibouris et al	Retrospective Cohort Study	61	2	11	2	2	-	-	-
Klopfenstein et al	Retrospective Cohort Study	114	19	55	25	9	-	-	-
Aghemo et al	Retrospective Cohort Study	325	-	69	-	11	-	-	54
Colaneri et al	Retrospective Cohort Study	44	-	3	-	-	-	-	-

Table. 6 Number of deaths reported among patients infected with SARS-CoV2

Study	Total no. of patients	Number of deaths(n)
Siegel et al	3	0
Pazgan-simon et al	1	0
Azwar et al	1	0
Jin, X et al	651	1
Nobel et al	278	9

Study	Total no. of patients	Number of deaths(n)
Lin et al	95	0
Zhou et al	254	16
Pan et al	204	36
Cholankeril et al	116	1
Fu et al	1	0
Li et al	1	1
Saeed et al	9	1
Arashiro et al.	1	1
Yang F et al	92	92
Chen Q et al	9	0
Huang, C et al	41	6
Chen, N et al	99	11
Wang et al	138	6
Xu, X et al	62	0
Fan et al	148	1
Zhang, B et al	82	82
Huang Y et al	36	36
Wan, S et al	135	1
Zhang, Y et al	115	1
Xu, Z et al	1	1
Arentz et al	21	11
Kujawski et al	12	0
Young et al	18	0
Sun et al	54	2
Pung et al	36	0
Qian et al	91	0
Luo et al	183	7
Zhou F et al	191	54
Chen T et al	274	113
Shi S et al	416	30
Mao L et al	214	1
Ai JW et al	102	3
Liu Y et al	109	31
Shu L et al	545	0
Wei et al	100	3
Zhao W et al	77	5
Yang P et al	55	2
Qi D et al	267	4
Wen Y et al	417	3
Xu Y et al	45	1

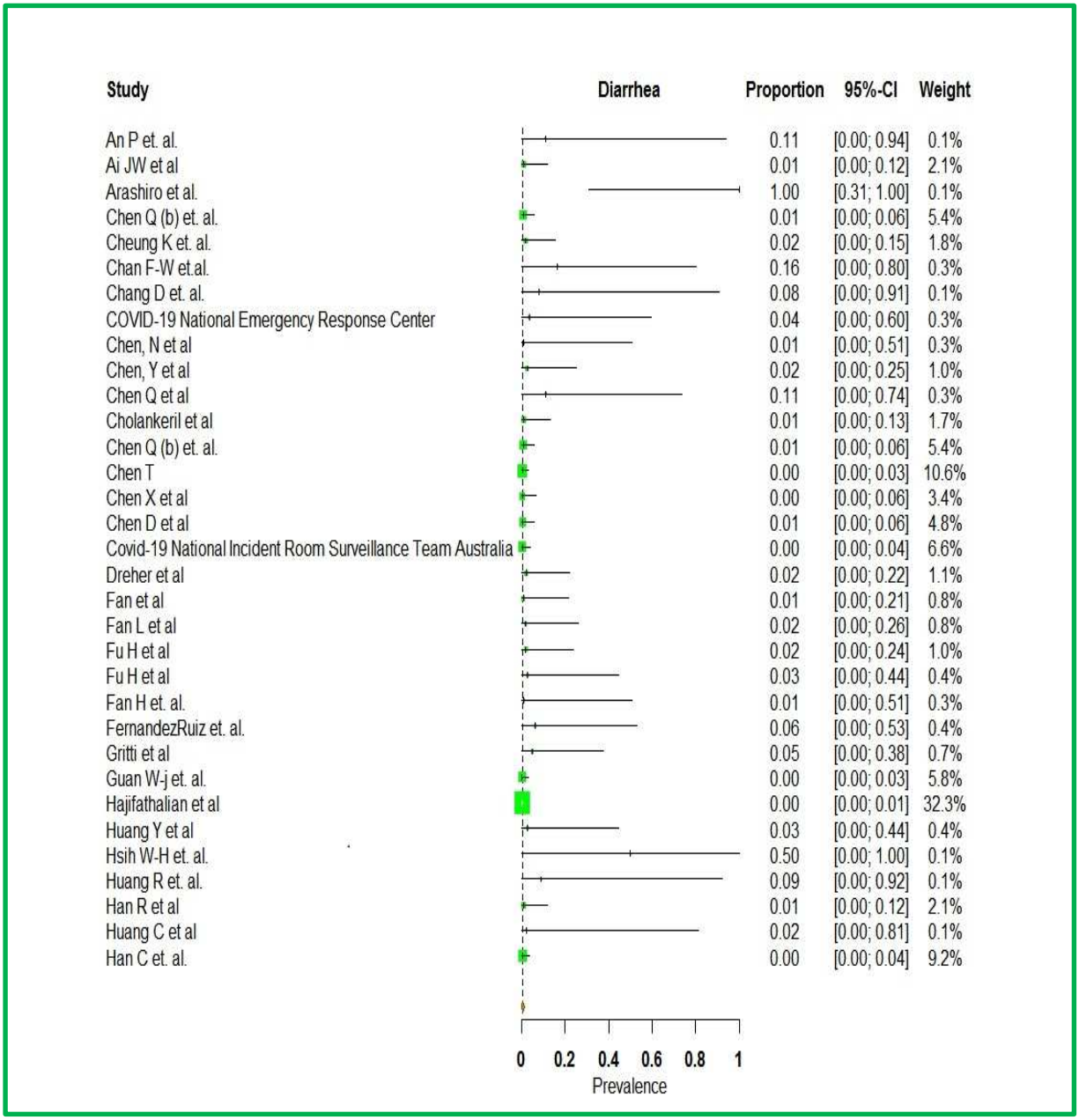
Study	Total no. of patients	Number of deaths(n)
Yan S et al	168	6
Wang L et al	18	0
Chen X et al	291	2
Liu S et al	620	0
Tian S et al	37	0
Lu H et al	265	1
Fu H et al	52	0
Pung et al	17	0
Dreher et al	50	7
Gritti et al	21	1
Spiteri et al	38	1
Covid-19 National Incident Room Surveillance Team Australia	295	3
Sulaiman et al.	140	12
Ferm et al	892	215
Ramachandran et al	150	45
Suleyman et al	463	15
Borobia A. et al.	2226	460
Massironi et al.	38	5
Livanos AE. et al.	634	47
Khader et al	1	0
Grande G et al	1	1
Gulen M et al	1	0
Cholankeril et al.	207	4
Cavaliere et al	6	0
Hassani AH et al.	2	1
Wu CY et al	1	0
Wang K et al	2	1
Dietrich CG	1	0
Kandasamy S et al	1	0
Wagner J et al	99	16
Wahab SF et al	1	0
Cheung S et al	1	0
Moura DTH et al	400	89
A. Papa et al	34	9
N Aumpan et al.	40	0
Tsibouris et al	61	16
Docherty AB. et al.	16749	5527
Aghemo et al	325	56
Total	30148	7113

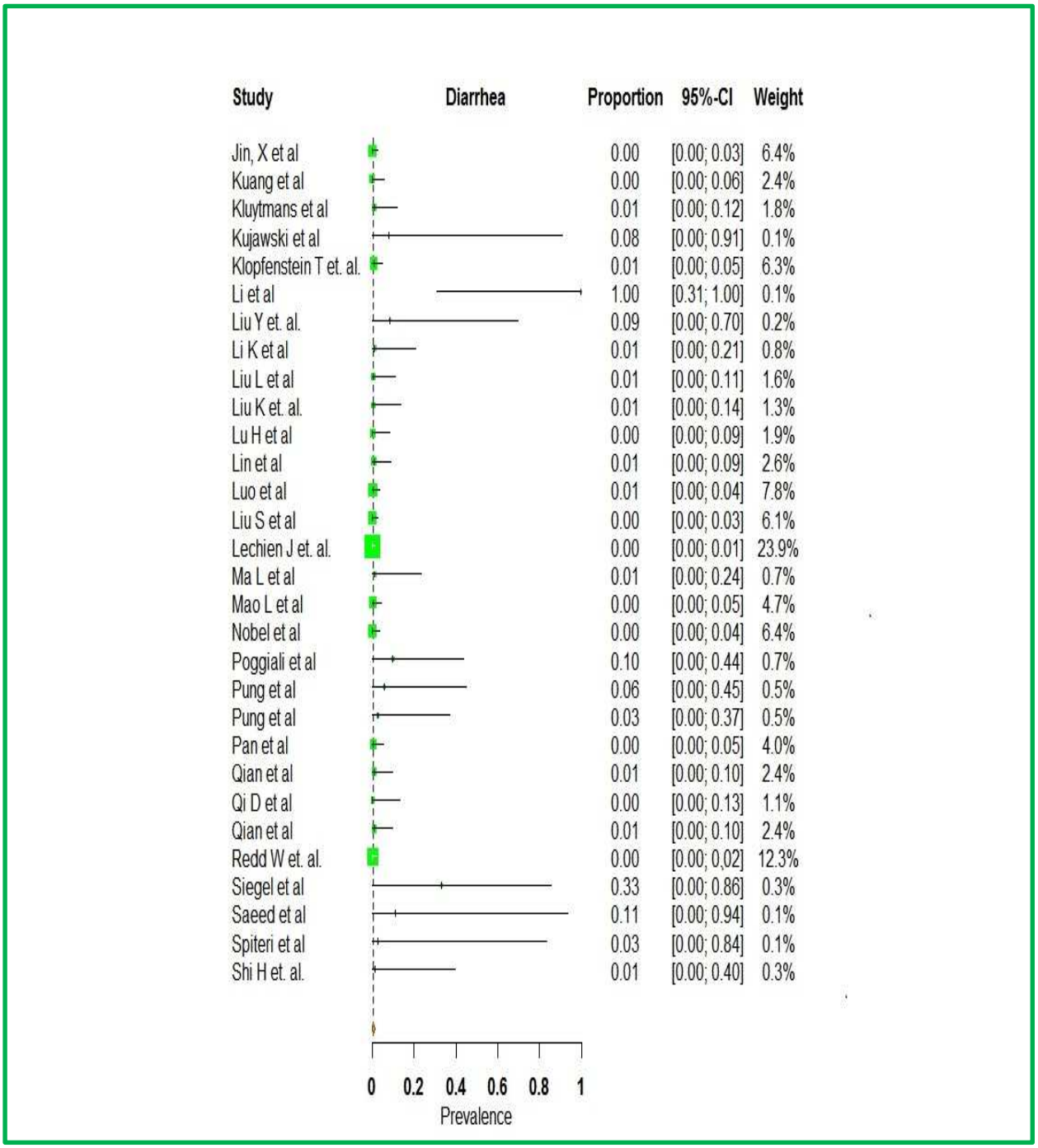
Table. 7 Number of deaths reported among patients infected with SARS-CoV2 who were experiencing GI symptoms/elevated liver enzymes

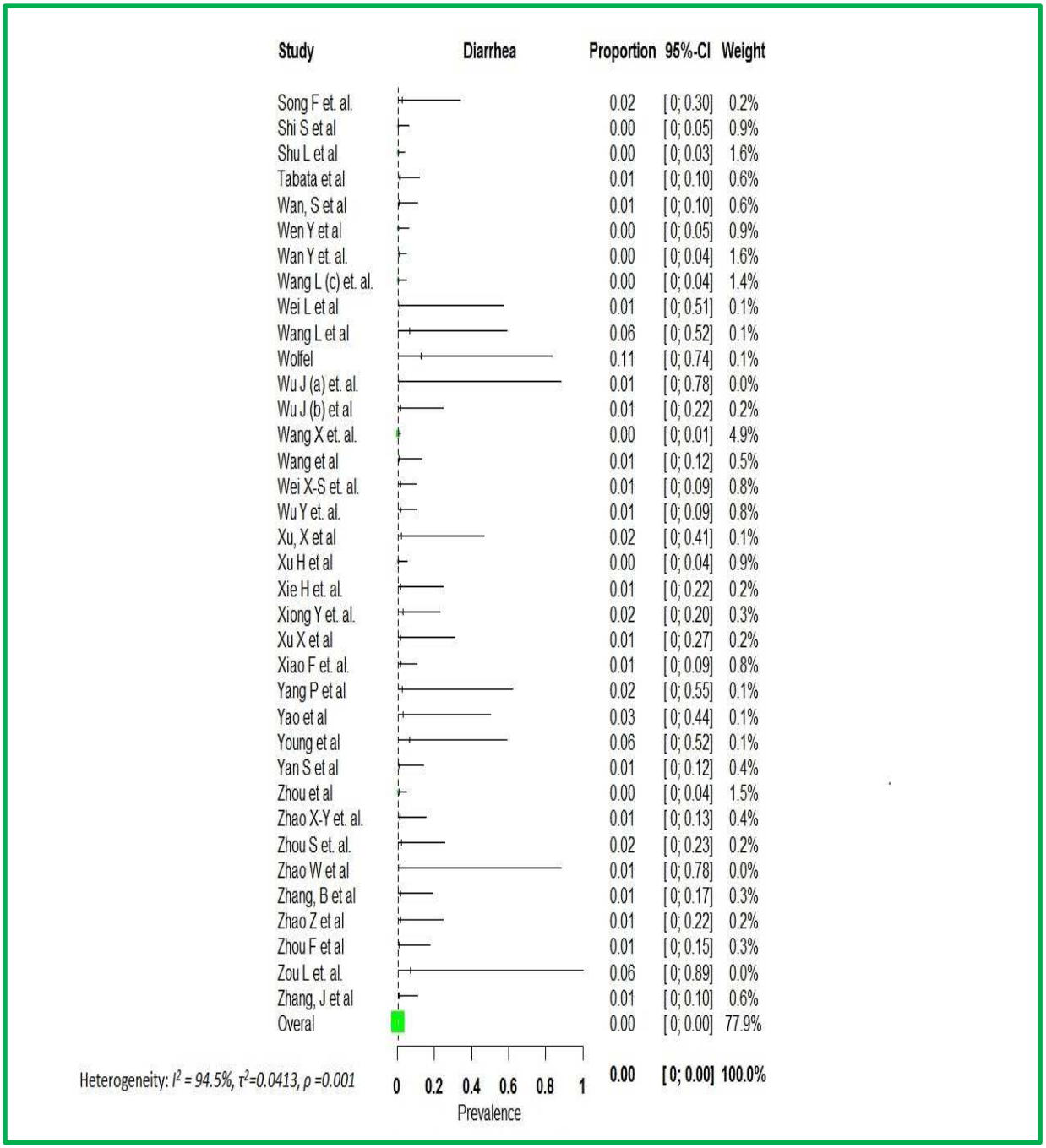
Study	Total no. of patients	Number of deaths in patients with GI symptoms
Fan H et. al.	101	9
Han C et. al.	206	0
Hsih W-H et. al.	2	0
Huang WH et. al.	2	0
Kuang Y et. al.	944	0
Kim ES et. al.	28	0
Shu L et. al.	545	0
Jin X et. al.	651	0
Lin L et. al.	95	0
Pan F et. al.	21	0
Zhao D et. al.	19	0
Redd W et. al.	318	16
Luo S et. al.	1141	7
Song F et. al.	51	0
Wan Y et. al.	230	4
Wei X-S et. al.	84	0
Wu Y et. al.	74	0
Zhou F et. al.	191	2
Zhou Z et. al.	254	5
Xia X et. al.	10	0
Sulaiman et al.	140	0
Ramachandran et al	150	13
Khader et al	1	0
Grande G et al	1	1
Gulen M et al	1	0
Cavaliere K et al	6	0
Hassani AH et al	2	1
Wu CY et al	1	0
Wang K et al	2	1
Dietrich et al	1	0
Kandasamy S et al	1	0
Wagner J et al	99	16
Wahab SF et al	1	0
Cheung S et al	1	0

Moura DTH et al	400	28
A. Papa et al	8	1
Tabata et al	104	0
Cholankeril G et. al.	116	0
Kujawski S et. al.	12	0
Redd W et. al.	318	16
Siegel et. al.	3	0
Laszkowska et al	1084	147
Total	7419	267

Supplementary figure.1 Forest plot depicting prevalence of diarrhea




Study
Diarrhea
Proportion
95%-CI
Weight
Jin, X et al 0.00 [0.00; 0.03] 6.4%
Kuang et al 0.00 [0.00; 0.06] 2.4%
Kluytmans et al 0.01 [0.00; 0.12] 1.8%
Kujawski et al 0.08 [0.00; 0.91] 0.1%
Klopfenstein T et. al. 0.01 [0.00; 0.05] 6.3%
Li et al 1.00 [0.31; 1.00] 0.1%
Liu Y et. al. 0.09 [0.00; 0.70] 0.2%
Li K et al 0.01 [0.00; 0.21] 0.8%
Liu L et al 0.01 [0.00; 0.11] 1.6%
Liu K et. al. 0.01 [0.00; 0.14] 1.3%
Lu H et al 0.00 [0.00; 0.09] 1.9%
Lin et al 0.01 [0.00; 0.09] 2.6%
Luo et al 0.01 [0.00; 0.04] 7.8%
Liu S et al 0.00 [0.00; 0.03] 6.1%
Lechien J et. al. 0.00 [0.00; 0.01] 23.9%
Ma L et al 0.01 [0.00; 0.24] 0.7%
Mao L et al 0.00 [0.00; 0.05] 4.7%
Nobel et al 0.00 [0.00; 0.04] 6.4%
Poggiali et al 0.10 [0.00; 0.44] 0.7%
Pung et al 0.06 [0.00; 0.45] 0.5%
Pung et al 0.03 [0.00; 0.37] 0.5%
Pan et al 0.00 [0.00; 0.05] 4.0%
Qian et al 0.01 [0.00; 0.10] 2.4%
Qi D et al 0.00 [0.00; 0.13] 1.1%
Qian et al 0.01 [0.00; 0.10] 2.4%
Redd W et. al. 0.00 [0.00; 0,02] 12.3%
Siegel et al 0.33 [0.00; 0.86] 0.3%
Saeed et al 0.11 [0.00; 0.94] 0.1%
Spiteri et al 0.03 [0.00; 0.84] 0.1%
Shi H et. al. 0.01 [0.00; 0.40] 0.3%
0
0.2
0.4
0.6
0.8
1
Prevalence


Study
Diarrhea
Proportion
95%-CI
Weight
Song F et. al. 0.02 [0; 0.30] 0.2%
Shi S et al 0.00 [0; 0.05] 0.9%
Shu L et al 0.00 [0; 0.03] 1.6%
Tabata et al 0.01 [0; 0.10] 0.6%
Wan, S et al 0.01 [0; 0.10] 0.6%
Wen Y et al 0.00 [0; 0.05] 0.9%
Wan Y et. al. 0.00 [0; 0.04] 1.6%
Wang L (c) et. al. 0.00 [0; 0.04] 1.4%
Wei L et al 0.01 [0; 0.51] 0.1%
Wang L et al 0.06 [0; 0.52] 0.1%
Wolfel 0.11 [0; 0.74] 0.1%
Wu J (a) et. al. 0.01 [0; 0.78] 0.0%
Wu J (b) et al 0.01 [0; 0.22] 0.2%
Wang X et. al. 0.00 [0; 0.01] 4.9%
Wang et al 0.01 [0; 0.12] 0.5%
Wei X-S et. al. 0.01 [0; 0.09] 0.8%
Wu Y et. al. 0.01 [0; 0.09] 0.8%
Xu, X et al 0.02 [0; 0.41] 0.1%
Xu H et al 0.00 [0; 0.04] 0.9%
Xie H et. al. 0.01 [0; 0.22] 0.2%
Xiong Y et. al. 0.02 [0; 0.20] 0.3%
Xu X et al 0.01 [0; 0.27] 0.2%
Xiao F et. al. 0.01 [0; 0.09] 0.8%
Yang P et al 0.02 [0; 0.55] 0.1%
Yao et al 0.03 [0; 0.44] 0.1%
Young et al 0.06 [0; 0.52] 0.1%
Yan S et al 0.01 [0; 0.12] 0.4%
Zhou et al 0.00 [0; 0.04] 1.5%
Zhao X-Y et. al. 0.01 [0; 0.13] 0.4%
Zhou S et. al. 0.02 [0; 0.23] 0.2%
Zhao W et al 0.01 [0; 0.78] 0.0%
Zhang, B et al 0.01 [0; 0.17] 0.3%
Zhao Z et al 0.01 [0; 0.22] 0.2%
Zhou F et al 0.01 [0; 0.15] 0.3%
Zou L et. al. 0.06 [0; 0.89] 0.0%
Zhang, J et al 0.01 [0; 0.10] 0.6%
Overal 0.00 [0; 0.00] 77.9%
Heterogeneity: I^2 = 94.5%, τ^2=0.0413, p =0.001
0.00 [0; 0.00] 100.0%
0 0.2 0.4 0.6 0.8 1
Prevalence

Supplementary figure.2 Mortality in patients experiencing GI symptoms/elevated liver enzymes