Systematic Review

Clinical, Laboratory and Imaging Features of COVID-19: A systematic review and meta-analysis

Alfonso J. Rodríguez-Morales,1,2,3,4,5,6,7,8 Jaime A. Cardona-Ospina,1,2,3,4,5,6,7,8 Estefanía Gutiérrez-Ocampo,9 Rhuvi Villamizar-Peña,1 Yeimer Holguín-Rivera,1 Juan Pablo Escalera-Anteza,1,9,10 Lucia Elena Alvarado-Arnez,6 D. Katterine Bonilla-Aldana,1,3,10 Carlos Franco-Paredes,4,11,12 Andrés F. Henao-Martínez,11 Alberto Paniz-Mondolfi,11,13,14,15,16 Guillermo J. Lagos-Grisales,1 Eduardo Ramírez-Vallejo,1 José A. Suárez,3,17 Lysien I. Zambrano,18 Wilmer E. Villamil-Gómez,3,4,19,20 Ali A. Rabaan,21 Harapan Harapan,22,23,24 Kuldeep Dhama,25 Hiroshi Nishiura,26 Hiromitsu Kataoka,27 Tauseef Ahmad,28,29 Ranjit Sah,30

1Public Health and Infection Research Group, Faculty of Health Sciences, Universidad Tecnológica de Pereira, Pereira, Risaralda, Colombia.
2Grupo de Investigación Biomedicina, Faculty of Medicine, Fundación Universitaria Autónoma de las Américas, Pereira, Risaralda, Colombia.
3Comité en Medicina Tropical, Zoonosis and Travel Medicine, Asociación Colombiana de Infectología, Bogotá, DC, Colombia.
4Committe on Travel Medicine, Pan-American Association of Infectious Diseases (API), Pereira, Risaralda, Colombia.
5Grupo de Investigación Infección e Inmunidad, Faculty of Health Sciences, Universidad Tecnológica de Pereira, Pereira, Risaralda, Colombia.
6Semillero de Investigación en Infecciones Emergentes y Medicina Tropical, Faculty of Medicine, Fundación Universitaria Autónoma de las Américas, Pereira, Risaralda, Colombia.
7Emerging Infectious Diseases and Tropical Medicine Research Group, Instituto para la Investigación en Ciencias Biomédicas – SCIHELP, Pereira, Risaralda, Colombia.
8Universidad Franz Tamayo/UNIFRANZ, Cochabamba, Bolivia.
9National Responsible for Telehealth Program, Ministry of Health, La Paz, Bolivia.
10Incubator in Zoonosis (SIZOO), Biodiversity and Ecosystem Conservation Research Group (BIOECOS), Fundación Universitaria Autónoma de las Américas, Sede Pereira, Pereira, Risaralda, Colombia.
11Division of Infectious Diseases, Department of Medicine, University of Colorado Anschutz Medical Center, Aurora, CO, USA.
12Hospital Infantil de México Federico Gómez, México City, Mexico.
13Laboratory of Medical Microbiology, Department of Pathology, Molecular and Cell-based Medicine, The Mount Sinai Hospital-Icahn School of Medicine at Mount Sinai, New York, USA.
14Laboratorio de Señalización Celular y Bioquímica de Parásitos, Instituto de Estudios Avanzados (IDEA), Caracas, Caracas, Venezuela.
15Academia Nacional de Medicina, Caracas, Venezuela.
16Instituto de Investigaciones Biomedicas IDB / Incubadora Venezolana de la Ciencia, Cabudare, Edo. Lara, Venezuela.
17Investigador SNI Senacryt Panamá, Clinical Research Departament, Instituto Conmemorativo Gorgas de Estudios de la Salud, Panamá City, Panama.
18Departments of Physiological and Morphological Sciences, School of Medical, Sciences, Universidad Nacional Autónoma de Honduras (UNAH), Tegucigalpa, Honduras.
Abstract

Introduction: An epidemic of Coronavirus Disease 2019 (COVID-19) begun in December 2019 in China, causing a Public Health Emergency of International Concern. Among raised questions, clinical, laboratory, and imaging features have been partially characterized in some observational studies. No systematic reviews have been published on this matter.

Methods: We performed a systematic literature review with meta-analysis, using three databases to assess clinical, laboratory, imaging features, and outcomes of confirmed cases of COVID-19. All the observational studies, and also case reports, were included, and analyzed separately. We performed a random-effects model meta-analysis to calculate the pooled prevalence and 95% confidence interval (95% CI). Measures of heterogeneity were estimated and reported.

Results: 660 articles were retrieved. After screening by abstract and title, 27 articles were selected for full-text assessment. Of them, 19 were finally included for qualitative and quantitative analyses. Additionally, 39 case report articles were included and analyzed separately. For 656 patients, fever (88.7%, 95% CI 84.5-92.9%), cough (57.6%, 40.8-74.4%) and dyspnea (45.6%, 10.9-80.4%) were the most prevalent clinical manifestations. Among the patients, 20.3% (95% CI 10.0-30.6%) required intensive care unit (ICU), with 32.8% presenting acute respiratory distress syndrome (ARDS) (95% CI 13.7-51.8), 6.2% (95% CI 3.1-9.3) with shock and 13.9% (95% CI 6.2-21.5%) with a fatal outcome.

Discussion: COVID-19 is a new clinical infectious disease, causing considerable compromise, especially in patients with comorbidities, requiring ICU in at least a fifth of them and sometimes with fatal outcomes. Additional research is needed to elucidate factors that may mediate the pathogenesis of the severe and fatal associated disease.

Keywords: Coronavirus Disease 2019; SARS-CoV-2; clinical features; laboratory; outcomes; epidemic.
Introduction

Rationale

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2, SARS2, 2019-nCoV or COVID-19 virus), is a newly emerging zoonotic agent appearing in December 2019. This pathogen causes a syndrome leading in some cases to a critical care respiratory condition, requiring specialized management at intensive care units (ICU) in many of them [1-6]. The SARS-CoV-2, taxonomically, is currently part of the species of the SARS-related coronaviruses that belong to the subgenus Sarbecovirus. Together with the subgenera Embecovirus, Hibecovirus, Merbecovirus, and Nobecovirus, that is part of the genus Betacoronavirus (order Nidovirales; suborder Coronavirinae; family Coronaviridae; subfamily Coronavirinae) [7-13].

Other Betacoronaviruses before have caused epidemics over the last two decades in Asia, as is the case of SARS-CoV in 2002-2003 in China [9, 14, 15], and later with the Middle East Respiratory Syndrome (MERS-CoV) in 2012-2013 in Saudi Arabia [16-19]. As expected, several similarities and differences in the epidemiology, clinical features, and management of SARS, MERS, and COVID have been identified [2-4, 19-22]. These are enveloped positive-strand RNA viruses isolated from bats that share sequence homology with isolates from humans, suggesting them as natural hosts and reservoirs [8, 23-26]. Although the clinical picture of SARS, MERS, and COVID seems to be similar, since early reports, differences were noted [3, 4, 20, 27]. Then, full clinical characterization of disease, as well as their laboratory and image findings, is required.

While, two months after the beginning of the COVID-19, is still a preliminary time frame, some studies and case reports have been already published in major international scientific and medical journals, from China and other countries with travel- and non-travel-related cases [6, 12, 28, 29]. Many of them alone started to answer clinical questions, including evolution and outcomes, as well as potential risk factors, and clinical, laboratory and image findings; however, a systematic review to consolidate what has been learned from each study or reported case is still required.

Objectives

• To summarize the clinical, laboratory, and image features of COVID-19 reported on currently available observational studies
• To examine the outcome of COVID-19 cases, including risk factors, the proportion of patients requiring ICU and those evolving to death.
• To assess the prevalence of comorbidities among COVID-19 confirmed cases, and the causality link between fatal cases and SARS-CoV-2

Methods

Protocol and registration
This protocol follows the recommendations established by the PRISMA statement [30], and it has been reported in the PROSPERO database (ID 170643).

Eligibility criteria

We included published peer-reviewed articles that reported cases with demographical, clinical, laboratory, and image features of RT-PCR confirmed SARS-CoV-2 infection. For assessing clinical, laboratory and imaging characteristics eligible study designs were case-control, cohort studies, case reports, and case series. For assessing risk factors and outcomes only observational studies were included. For causality link assessment, all included articles were used. Article language limit was not set, and we included publications from January 1, 2020 until the date the search was finished. Review articles, opinion articles and letters not presenting original data were excluded, as well as studies reporting cases with incomplete information.

Information sources and Search Strategy

We conducted a systematic review using Medline/PubMed, Scopus, and Web of Sciences. The search terms used were these: “Novel coronavirus,” “Novel coronavirus 2019”, “2019 nCoV”, “COVID-19”, “Wuhan coronavirus,” “Wuhan pneumonia,” and “SARS-CoV-2.” The searches were concluded by February 23, 2020, and four different researchers independently evaluated search results.

Study Selection

The results of the initial search strategy were first screened by title and abstract. The full texts of relevant articles were examined for inclusion and exclusion criteria (Figure 1). When an article reported duplicate information from the same patient, the information of both reports was combined in order to obtain complete data, but only counted as a single case. Observational studies that reported the proportion of symptoms, laboratory characteristics and risk factors were included for quantitative synthesis (metanalysis).

Data collection process and data items:

Data extraction forms including information on the type of publication, the publishing institution, country, year and date of publication, the number of reported cases, of cases at ICU, age, sex, comorbidities, clinical features (e.g., fever, cough), laboratory findings (e.g., WBC, biochemistry), imaging (e.g., chest X-ray), complications (e.g., ARDS), outcome (e.g., death) were filled independently by four investigators. A fifth researcher checked the article list and data extractions to ensure there were no duplicate articles or duplicate information of the same patient and also resolved discrepancies about study inclusion.

Assessment of methodological quality and risk of bias:
For quality assessment, we used the Quality Appraisal of Case Series Studies Checklist of the IHE and specifically the critical appraisal tool to assess the quality of cross-sectional studies (AXIS) [31, 32]. Publication bias was assessed using a funnel-plot. A random-effects model was used to calculate the pooled prevalence and 95% CI, given variable degrees of data heterogeneity, and given the inherent heterogeneity in any systematic review of studies from the published literature. Also, Egger’s test was performed.

Statistical approach

Unit discordance for variables was resolved by converting all units to a standard measurement for that variable. Percentages and means ± standard deviation (SDs) were calculated to describe the distributions of categorical and continuous variables, respectively. Since individual patient information was not available for all patients, we report weighted means and SDs. The baseline data were analyzed using the Stata version 14.0, licensed for Universidad Tecnológica de Pereira.

The meta-analyses were performed using Stata, and the software OpenMeta[Analyst] [33] and Comprehensive Meta Analysis ve.3.3® licensed for Universidad Tecnológica de Pereira. Pooled prevalences and their 95% confidence intervals (95% CIs) were used to summarize the weighted effect size for each study grouping variable using the binary random-effects model (the weighting took into consideration the sample sizes of the individual studies), except for median age, where a continuous random-effect model was applied (DerSimonian-Laird procedure) [34, 35]. A random-effects meta-analysis model involves an assumption that the effects being estimated in the different studies are not identical, but follow some distribution. For random-effects analyses, the pooled estimate and 95%CIs refer to the center of the distribution of pooled prevalence but do not describe the width of the distribution. Often the pooled estimate and its 95%CI are quoted in isolation as an alternative estimate of the quantity evaluated in a fixed-effect meta-analysis, which is inappropriate. The 95%CI from a random-effects meta-analysis describes uncertainty in the location of the mean of systematically different prevalence in the different studies.

Measures of heterogeneity, including Cochran’s Q statistic, the I² index, and the tau-squared test, were estimated and reported. We performed subgroup analyses by age groups (adults or children). And meta-analyses for each of the variables of interest. Publication bias was assessed using a funnel-plot. A random-effects model was used to calculate the pooled prevalence and 95% CI, given variable degrees of data heterogeneity, and given the inherent heterogeneity in any systematic review of studies from the published literature.

Results

Study Selection and Characteristics:

A total of 660 articles were retrieved using the search strategy, including 39 case reports. After screening by abstract and title, 64 articles were selected for full-text assessment. Of these, six were excluded due to lack of information on molecular
diagnosis, and 58 were finally included for final qualitative analysis, 19 of them for quantitative meta-analysis and 39 case reports for descriptive analysis (Figure 1). The main characteristics of the included studies are shown in Table 1.

Our review included 19 studies that were published between January 1, 2020, and February 21, 2020, most of them from China (18) and one from Australia (Table 1), including a total of 2,874 patients, ranging from a case series of 9 [36] to a cross-sectional study of 1,590 [37]. Most studies were cross-sectional (15), and four were case series (Tables 1-5). We analyzed 42 variables for the meta-analyses (Table 6). Publication bias was assessed with a funnel plot for the standard error by logit event, with no evidence of bias (Figure S1). Additionally, the Egger test (P=0.801) suggested that there was no notable evidence of publication bias.

Demographical characteristics and comorbidities:

The mean age of patients across 18 studies was 51.97 years old (95%CI 46.06-57.89), being male 55.9% (95%CI 51.6-60.1%). Patients presented in 36.8% comorbidities (95%CI 24.7-48.9%), being the highest hypertension (18.6%, 95%CI 8.1-29.0%), cardiovascular disease (14.4%, 95%CI 5.7-23.1%), and diabetes (11.9%, 95%CI 9.1-14.6%), among others (Table 6) (Figure S2).

Clinical manifestations and laboratory findings:

Regarding the clinical manifestations, fever (88.7%, 95%CI 84.5-92.9%), cough (57.6%, 40.8-74.4%) and dyspnea (45.6%, 10.9-80.4%) were the most prevalent clinical manifestations (Table 6). Fever frequency was significantly higher in adults compared to children (92.8%, 95%CI 89.4-96.2%; versus 43.9%, 95%CI 28.2-59.6%) (Figure S2).

Concerning laboratory findings, decreased albumin (75.8%, 95%CI 30.5-100.0%), high C-reactive protein (58.3%, 95%CI 21.8-94.7%), and high lactate dehydrogenase (LDH) (57.0%, 95%CI 38.0-76.0), lymphopenia (43.1%, 95%CI 18.9-67.3), and high erythrocyte sedimentation rate (ESR) (41.8%, 95%CI 0.0-92.8), were the most prevalent (Table 6) (Figure S2).

Imaging, Complications, and Outcomes:

At the chest X-rays, the pneumonia compromise was predominantly bilateral (72.9%, 95%CI 58.6-87.1), being the image findings ground-glass opacity in 68.5% (95%CI 51.8-85.2) (Table 6) (Figure S2).

Among the patients, 20.3% (95%CI 10.0-30.6%) required ICU, with 32.8% presenting ARDS (95%CI 13.7-51.8), 13.0% acute cardiac injury (95%CI 4.1-21.9%), 7.9% acute kidney injury (95%CI 1.8-14.0%), 6.2% (95%CI 3.1-9.3%) with shock and with a fatal outcome in 13.9% (95%CI 6.2-21.5%) (Table 6). RNAemia was reported 96.8% of the patients (95%CI 94.9-98.7%) (Table 6) (Figure S2).

Case reports:
We found 39 case report articles (Table S1, summarizing 126 cases of COVID-19. The mean age was 47.9 y-old (SD 22.2), being male 69.01% of those with sex identified in the article (Table 7). From the total, 10.3% presented hypertension as comorbidity, followed by other conditions. The more common clinical features were fever (77.0%), cough (55.6%), and myalgia (31.0%), among others (Table 7). Regarding the laboratory findings, lymphopenia was the more frequent (23.8%), followed by high C-reactive protein (22.2%) and high aspartate transaminase (AST) (7.9%). At the chest X-ray, 46% presented ground-glass opacity, with a bilateral compromise in 39.7% of the patients. All the case reports had RNAaemia. For the complications, 7.1% presented ARDS, and 1.6% secondary infections, among others. Most of the case reports were hospitalized (74.6%), with a fatality rate of 15.9% (Table 7).

Discussion

Over the last two months, more than 85,000 cases of a new infectious disease have been confirmed in China and other countries in Asia, Europe, Africa, and the Americas [21, 22, 38-40]. The COVID-19 is an emerging condition that primarily threat the preparedness and biosecurity conditions of the countries in the world [41]. Preparedness at different levels, facing a new clinical disease, demands efforts in epidemiological, diagnostic, therapeutic, and preventive fields during a potential pandemic [42], which threat with spread to new territories and areas with the risk of epidemics.

Clinical, laboratory, image findings, as well as the factors associated with evolution and outcomes, are critical knowledge that should be carefully studied when a new infectious disease emerged, including multiple other factors. Recently, in this context of the COVID-19 outbreak, several questions have been raised, including what is the full spectrum of disease severity (which can range from asymptomatic, to symptomatic-but-mild, to severe, to requiring hospitalization, to fatal)? [43]. In this systematic review, we tried to initially summarize clinical data on COVID-19 confirmed cases that were published over the first weeks of the outbreak, achieving to analyze more than 780 patients for major clinical manifestations, and close to a half of them for identifying significant laboratory findings.

As expected from initial observations in China [3, 4, 10], COVID-19 patients presented predominantly with fever and cough, which appears to be more frequent in adults than children, as well as dyspnea, and myalgia, among other clinical features. This was consistently found not only in the studies meta-analyzed but also in the case reports included in this systematic review. Fever frequency is similar in SARS and MERS, but the cough is higher in SARS and COVID-19 than MERS (<50%) [27, 44, 45]. In SARS and MERS, diarrhea is reported in 20-25% of patients [46], here we found it in less than 7%, at the studies (Table 6) and case reports (Table 7). Curiously, at case reports, myalgia was the third most common reported symptom after fever and cough. Most patients required hospitalization, which can be explained due to the patient’s previous comorbidities, observed in a third of the cases. Then, also requiring in a fifth of them, to be admitted to ICU for critical management. Unlike what happens in SARS, with the well-characterized two-stages clinical course of the disease, in COVID-19, still, this needs further definition [44]. A first week is also similar, coinciding with recent data of the viral load during this stage [47]. However, case-control studies and cohort studies are necessary to define the clinical evolution of disease better.
A second stage, as occurs in SARS, is maybe also seen in COVID-19, with the lower respiratory tract bilateral compromise, observed in more than 72% of the patients across nine studies with more than 500 patients, also experiencing a dry cough, and dyspnea [4, 44, 48] and with images at chest X-rays of ground-glass opacity frequently observed, two-thirds of patients, which is also seen in SARS.

The laboratory alterations predominantly found include hypoalbuminemia, elevated inflammatory markers, such as C-reactive protein, LDH, and ESR, among others. Also, lymphopenia is consistently present in more than 40% of the patients across eight studies with more than 500 patients. Data from the 2002-2003 outbreak indicate that SARS may be associated with lymphopenia, leukopenia, and thrombocytopenia, elevated levels of LDH, alanine transaminase (ALT), AST, and creatine kinase [49, 50], but also, and not significantly seen, nor consistently reported, in COVID-19 studies and cases, with thrombocytopenia, mild hyponatremia, and hypokalemia. The frequency of lymphopenia found suggests that COVID-19 might act on lymphocytes, especially T lymphocytes, as does SARS-CoV [3]. Virus particles spread through the respiratory mucosa, initially using the ACE2 receptor at ciliated bronchial epithelial cells, and infect other cells, induce a cytokine storm in the body, generate a series of immune responses, and cause changes in peripheral white blood cells and immune cells such as lymphocytes [51, 52].

Patients complicated and died. A third of them presented ARDS, but also, albeit in a lower frequency, acute cardiac injury, acute kidney injury, and shock, eventually followed by multiple organ failure. Therefore, early identification and timely treatment of critical cases are of crucial importance [3]. They evolved in more than 13% to a fatal outcome in 7 studies summarizing 632 patients. In two studies in China (n=41, n=99), the case fatality rates were 15% [4] and 11% [3], respectively. Crude surveillance data [38], indicated that till February 29, 2020, from 85,688 reported cases, 2,993 patients have died (3.42%), with >90% of the deaths occurred in China. Nevertheless, after all, more studies are needed to answer what the risk factors for severe illness or death are? Moreover, how can we identify groups most likely to have poor outcomes so that we can focus on prevention and treatment efforts? [43].

After the development of this systematic review (SR), and even availability on a preprint server, online Feb. 25, 2020 (http://dx.doi.org/10.20944/preprints202002.0378.v1); a brief systematic review and meta-analysis, only addressing fever, cough, muscle soreness or fatigue, ARDS, abnormal chest CT, patients in critical condition and death of patients with COVID-19, was published (Feb. 28, 2020) [53]. This review was based on ten studies, using a random effect model, as we did.

Comparing their findings [53] with ours, they found fever in 89.8% (95%CI 81.8-94.5%) of patients, this SR found 88.7% (95%CI 84.5-92.9%), but we assessed differences, as mentioned above, between adults and children, and they not. For cough, based on the 95%CI, there were not significant differences too, between that SR and the current, 72.2% (95%CI 65.7-78.2%) versus 57.6% (95%CI 40.8-74.4%). For fatigue, also there is overlapping in the frequency between both studies, 42.5% (95%CI 21.3-65.2%) versus 29.4% (95%CI 19.8-39.0%). Sun et al did not assessed other clinical manifestations [53], we were able to do it for eight of them. Between both reviews is clear and consistent that more than 80% of the patients presented
fever, more than a half cough, and more than a third fatigue. That SR did not assess any laboratory findings, but evaluated the frequency of patients presenting ADRS, 14.8% (95% CI 4.6-29.6%), which was also consistent with our study, 32.8% (95% CI 13.7-51.8%), although little higher, but with the 95% CI overlapping (not significant difference).

For patients in critical care, there were also small differences. Sun et al found 18.1% (95% CI 12.7-24.3%) and we 20.3% (95% CI 10.0-30.6%). The major difference between both studies was in the last variable assessed in that SR, deaths, they report 4.3% (95% CI 2.7-6.1%) and we 13.9% (95% CI 6.2-21.5%), being significantly lower compared with the current data. Finally, Sun et al only included studies, but not case reports, as we did, which provided additional consistent findings of the clinical, laboratory, imaging and evolution characteristics of patients with confirmed COVID-19.

Our results showed that there is still a need for more comprehensive clinical studies, including short and long-term follow-up cohort assessments. More studies related to outside, where there are more than 100 patients diagnosed with COVID-19, as is the case of South Korea, Italy, and Japan [54, 55], will be excellent opportunities also for this, in addition to the growing number of studies appearing from China. Even more, the situation with the cruise ship Diamond Princess, docked in Yokohama, Japan, with 3,711 passengers, approximately 20% of the infected, is also a valuable chance to characterize better the COVID-19. Clinical evidence synthesized in this review is mainly derived from China, although for case reports, ten of the thirty-two countries with confirmed cases [6, 11, 28, 29], have published some of them (Table 7). Then, would be good also have clinical data, from single case, or case series reports from Italy, which only have reported genomic data of their two first cases [56], Singapore, Hong Kong, which collaborated in the diagnosis of the unique case confirmed and published from Nepal [6], Iran, and Malaysia, among others with less than 20 cases, so far. Regardless, cross-sectional studies or case reports, the clinical findings were consistent between them but still limited to characterize further and define the risk factors for admission in ICU and fatal outcomes. However, data suggest that older age and comorbidities play a vital role in influencing severe disease and negative clinical outcomes. These data would be useful to guide patient risk groups management in the current epidemic, especially in those countries not yet receiving cases, as occur in many countries in Latin America, which only have confirmed COVID-19 cases in Brazil, Mexico and Ecuador, so far (February 29, 2020) [57]. In these and other resource-constrained settings, supplies chains, including those for drugs, would be even affected.

The results of this systematic review highlight the clinical, laboratory, and imaging findings that may assist clinicians anywhere in the globe in suspecting the possibility of COVID-19 infection in those with recent travel to areas with ongoing transmission or among contacts to a confirmed case. Early recognition of cases will allow clinicians to ensure adequate clinical monitoring, institution of supportive interventions, and preventing further transmission by implementing of infection control measures [28, 51, 58]. Finally, there is a need for prospective studies to further understand the epidemiology, pathogenesis, duration of viral shedding, and the clinical spectrum of disease associated to this emerging viral infection [28, 51, 58].

Knowledge of disease, as derived from studies and their synthesis, are of utmost importance not only for an appropriate clinical suspicion, diagnosis, management and prevention of COVID-19, but also support proper protection of the healthcare
workers in the face of arrival and spreading of this coronaviral disease in the countries through travellers and secondary autochthonous community transmission.

Limitations

This review has several limitations. First, still few studies are available for inclusion. It would be better to include as many studies not only from China, once these have been published, to get a more comprehensive understanding of COVID19. Second, more detailed patient information, particularly regarding clinical outcomes, was unavailable in most studies at the time of analyses; however, the data in this review permit a first synthesis of the clinical and laboratory characteristics of COVID-19, although the need to be more detailed for image characterization.

Conclusions

Infection with COVID-19 is associated with significant morbidity especially in patients with chronic medical conditions. At least one fifth of cases require supportive care in medical intensive care units. Despite the implementation of optimal supportive interventions, case fatality rate is more than 10 percent. Similar to other viral respiratory pathogens, COVID-19 presents in the majority of cases with a rapidly progressive course of fever, cough and dyspnea. One important distinguishing factor from is leukopenia and the rapid progression to ARDS. Eliciting a history of recent travel to areas with ongoing outbreaks of this emerging pathogen or contact with a confirmed case of COVID-19, should prompt clinicians to initiate isolation precautions and obtaining laboratory confirmation. Additional research is needed to elucidate viral and host factors in the pathogenesis of severe and fatal infections.

Acknowledgments. None.

Author Contributions. AJRM and JACO formulated the research questions, designed the study, developed the preliminary search strategy, and drafted the manuscript. EGO, RV, YHR refined the search strategy by conducting iterative database queries and incorporating new search terms. EGO, RV, YHR, and AJRM searched and collected the articles. JACO, AJRM, and DKBA conducted the quality assessment. All authors critically reviewed the manuscript for relevant intellectual content. All authors have read and approved the final version of the manuscript.

Conflicts of interest. All authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential.

Funding Source. Universidad Tecnológica de Pereira. Study sponsors had no role in the study design, in the collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

Ethical Approval. Approval was not required.

References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020 doi 10.1056/NEJMoa2001017.
2. Chan JF-W, Yuan S, Kok K-H, To KK-W, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. The Lancet. 2020 doi 10.1016/S0140-6736(20)30154-9.
3. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet. 2020 doi:10.1016/S0140-6736(20)30211-7.

4. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020;395:497-506.

5. The L. Emerging understandings of 2019-nCoV. The Lancet. 2020 doi:10.1016/S0140-6736(20)30186-0;395:311.

6. Bastola A, Sah R, Rodríguez-Morales AJ, Lal BK, Jha R, Ojha HC, et al. The first 2019 novel coronavirus case in Nepal. Lancet Infect Dis. 2020.

7. Bonilla-Aldana DK, Villamil-Gómez WE, Rabaan AA, Rodríguez-Morales AJ. Una nueva zoonosis viral de preocupación global: COVID-19, enfermedad de coronavirus 2019. Jatrea. 2020;33.

8. Millán-Orfate J, Rodríguez-Morales AJ, Camacho-Moreno G, Mendoza-Ramírez H, Rodríguez-Sabogal IA, Álvarez-Moreno C. A new emerging zoonotic virus of concern: the 2019 novel Coronavirus (COVID-19). Infectio 2020;24.

9. Ksiazek TG, Erdman D, Goldsmith CS, Zaki SR, Peret T, Emery S, et al. A novel coronavirus associated with severe acute respiratory syndrome. N Engl J Med. 2003;348:1953-66.

10. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med. 2020.

11. Phan LT, Nguyen TV, Luong QC, Nguyen TV, Nguyen HT, Le HQ, et al. Importation and Human-to-Human Transmission of a Novel Coronavirus in Vietnam. N Engl J Med. 2020 doi:10.1056/NEJMc2001272.

12. Pongpirul WA, Pongpirul K, Ratnarathon AC, Prasithsirikul W. Journey of a Thai Taxi Driver and Novel Coronavirus. N Engl J Med. 2020.

13. Gorbalenya AE. Severe acute respiratory syndrome-related coronavirus — the species and its viruses, a statement of the Coronavirus Study Group. bioRxiv. 2020:2020.02.07.937862.

14. Drosten C, Günther S, Preiser W, van der Werf S, Brodt HR, Becker S, et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. N Engl J Med. 2003;348:1967-76.

15. Kuiken T, Fouchier RA, Schutten M, Rimmelzwaan GF, van Amerongen G, van Riel D, et al. Newly discovered coronavirus as the primary cause of severe acute respiratory syndrome. Lancet. 2003;362:263-9.

16. de Wit E, van Doremalen N, Faalzarano D, Munster VJ. SARS and MERS: recent insights into emerging coronaviruses. Nat Rev Microbiol. 2016;14:523-34.

17. Al-Tawfiq JA, Gautret P. Asymptomatic Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection: Extent and implications for infection control: A systematic review. Travel Med Infect Dis. 2019;27:27-32.

18. Baaharoob S, Memish ZA. MERS-CoV as an emerging respiratory illness: A review of prevention methods. Travel Med Infect Dis. 2019;101520.

19. Bonilla-Aldana DK, Quintero-Rada K, Montoya-Posada JP, Ramírez S, Paniz-Mondolfi A, Rabaan A, et al. SARS-CoV, MERS-CoV and now the 2019-nCoV: Have we investigated enough about coronaviruses? - A bibliometric analysis. Travel Med Infect Dis. 2020:101566.

20. Al-Tawfiq JA, Zumla A, Memish ZA. Travel implications of emerging coronaviruses: SARS and MERS-CoV. Travel Med Infect Dis. 2014;12:422-8.

21. World Health Organization. Novel Coronavirus (2019-nCoV) - Situation report - 10 - 30 January 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200130-sitrep-10-ncov.pdf?sfvrsn=d0b2e48b_2_2.

22. World Health Organization. Pneumonia of unknown cause – China. https://www.who.int/csr/don/05-january-2020-pneumonia-of-unknown-cause-china/en/.

23. Rodríguez-Morales AJ, Bonilla-Aldana DK, Balbin-Ramon GJ, Paniz-Mondolfi A, Rabaan A, Sah R, et al. History is repeating itself, a probable zoonotic spillover as a cause of an epidemic: the case of 2019 novel Coronavirus. Infecz Med. 2020;28:3-5.

24. Bonilla-Aldana DK, Suarez JA, Franco-Paredes C, Vilcarromero S, Mattar S, Gomez-Marin JE, et al. Brazil burning! What is the potential impact of the Amazon wildfires on vector-borne and zoonotic emerging diseases? - A statement from an international experts meeting. Travel Med Infect Dis. 2019;31:101474.

25. Mattar S, González M. Zoonotic emergence of coronavirus: A potential public risk for Latin America. Rev MVZ Cordoba. 2018;2020.

26. Whitley R, Aloia F, Ramírez S, Paniz-Mondolfi A, Rabaan A, et al. Zoonoses and emerging infections: The emerging threat of severe acute respiratory syndrome coronavirus (SARS-CoV). Emerg Infect Dis. 2019;25:623-6.

27. Yin Y, Wunderink RG. MERS, SARS and other coronaviruses as causes of pneumonia. Respirology. 2018;23:130-7.

28. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, et al. First Case of 2019 Novel Coronavirus in the United States. N Engl J Med. 2020.

29. Silverstein WK, Stroud L, Clegheorn GE, Leis JA. First imported case of 2019 novel coronavirus in Canada, presenting as mild pneumonia. The Lancet. 2020.

30. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6:e1000097.

31. Institute of Health Economics (IHE). Quality Appraisal of Case Series Studies Checklist. Edmonton (AB): Institute of Health Economics; 2014.

32. Downes MJ, Brennan ML, Williams HC, Dean RS. Development of a critical appraisal tool to assess the quality of cross-sectional studies (AXIS). BMJ Open. 2016;6:e011458.

33. Wallace B, Dahabreh IJ, Trikalinos T, Ioannidis JPA. A bibliometric analysis. Travel Med Infect Dis. 2019;2020.

34. Viechtbauer W. Conducting meta-analyses in R with the metafor package. Journal of statistical software. 2010.

35. Kontopantelis E, Reeves D. Performance of statistical methods for meta-analyses: the PRISMA statement. PLoS Med. 2009;6:e1000097.

36. Whitaker R, Whitley R, Aloia F, Ramírez S, Paniz-Mondolfi A, Rabaan A, et al. Zoonoses and emerging infections: The emerging threat of severe acute respiratory syndrome coronavirus (SARS-CoV). Emerg Infect Dis. 2019;25:623-6.

37. Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol. 2020.

38. Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infect Dis. 2020.

39. World Health Organization. Statement on the meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). https://www.who.int/news-room/detail/23-01-2020-statement-on-the-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-nCoV). 2020.
40. World Health Organization. Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). https://www.who.int/news-room/detail/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov). 2020.

41. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, et al. A new coronavirus associated with human respiratory disease in China. Nature. 2020.

42. Paules CI, Marston HD, Fauci AS. Coronavirus infections—More Than Just the Common Cold. JAMA. 2020.

43. Lipshitz M, Swerdlow DL, Finelli L. Defining the Epidemiology of Covid-19—Studies Needed. N Engl J Med. 2020.

44. Srikantiah P, Charles MD, Reagan S, Clark TA, Pletz MW, Patel PR, et al. SARS clinical features, United States, 2003. Emerg Infect Dis. 2005;11:135-8.

45. de Groot RJ, Baker SC, Baric RS, Brown CS, Drosten C, Enjuanes L, et al. Middle East respiratory syndrome coronavirus (MERS-CoV): announcement of the Coronavirus Study Group. J Virol. 2013;87:7790-2.

46. Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. Lancet. 2020.

47. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. N Engl J Med. 2020.

48. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhu, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020.

49. Lee N, Hui D, Wu A, Chan P, Cameron P, Joynt GM, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. N Engl J Med. 2003;348:1986-94.

50. Tsang KW, Ho PL, Ooi GC, Yee WK, Wang T, Chan-Yeung M, et al. A cluster of cases of severe acute respiratory syndrome in Hong Kong. N Engl J Med. 2003;348:1977-85.

51. Rodriguez-Morales AJ, MacGregor K, Kanagarajah S, Patel D, Schlagenhaufl P. Going global - Travel and the 2019 novel coronavirus. Travel Med Infect Dis. 2020;33:101578.

52. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020.

53. Sun P, Qie S, Liu Z, Ren J, Li K, Xi J. Clinical characteristics of 50466 hospitalized patients with 2019-nCoV infection. J Med Virol. 2020.

54. Nishiura H, Kobayashi T, Yang Y, Hayashi K, Miyama T, Kinoshita R, et al. The Rate of Underascertainment of Novel Coronavirus (2019-nCoV) Infection Using Japanese Passengers Data on Evacuation Flights. J Clin Med. 2020;9.

55. Ishikawa H, Shimogawara R. Risk Assessment of Dengue Autochthonous Infections in Tokyo during Summer, Especially in the Period of the 2020 Olympic Games. Jpn J Infect Dis. 2019;72:399-406.

56. Giovanetti M, Benvenuto D, Angeletti S, Ciccozzi M. The first two cases of 2019-nCoV in Italy: Where they come from? J Med Virol. 2020.

57. Rodriguez-Morales AJ, Gallego V, Escalera-Antezana JP, Mendez CA, Zambrano L, Franco-Paredes C, et al. COVID-19 in Latin America: The implications of the first confirmed case in Brazil. Travel Medicine and Infectious Disease. 2020;101613.

58. Biscayart C, Angeleri P, Lloveras S, Chaves T, Schlagenhauf P, Rodriguez Morales AJ. The implications of the first confirmed case in Brazil. Travel Medicine and Infectious Disease. 2020;101613.

59. 旅行と2019新型コロナウイルス感染症．旅行医学協会．Health and Travel．第135号．2020年2月号．

60. Chung M, Bernheim A, Mei X, Huang M, Zeng X, et al. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV) Infection: Estimation Using Japanese Passengers Data on Evacuation Flights. J Clin Med. 2020;9.

61. Chen L, Liu HG, Liu W, Liu J, Liu K, Shang J, et al. Analysis of CT features of 15 Children with 2019 novel coronavirus infection. J Med Virol. 2020.

62. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus Infection in Wuhan, China. Radiology. 2020;200370.

63. Kui L, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chin Med J (Engl). 2020.

64. Chang, Lin M, Wei L, Xie L, ZHU G, DELA CRUZ CS, et al. Epidemiologic and Clinical Characteristics of Novel Coronavirus Infections Involving 13 Patients Outside Wuhan, China. JAMA. 2020.

65. To KK, Tsang OT, Chik YL, Yip WY, Ng SM, Poon LS, et al. A novel pneumonia associated with a new coronavirus of probable bat origin. Nature. 2020.

66. Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, et al. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). Radiology. 2020;200230.

67. Chen L, Liu HG, Liu W, Liu J, Liu K, Shang J, et al. Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. Zhonghua Jie He He Hu Xi Za Zhi. 2020;43:E005.

68. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. Eur Radiol. 2020.

69. Liu Y, Zhang D, Tang S, Chen H, Chen M, et al. The Epidemiological and Clinical Characteristics of 2019 Novel Coronavirus Infection in Changsha, China. Chin Med J (Engl). 2020;133:210-6.

70. Pan Y, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time Course of Lung Changes On Chest CT During Recovery From 2019 Novel Coronavirus (COVID-19) Infection. Radiology. 2020;200370.

71. Feng K, Yun YX, Wang XF, Yang GD, Zheng YJ, Lin CM, et al. [Analysis of CT features of 15 Children with 2019 novel coronavirus infection]. Zhonghua Er Ke Za Zhi. 2020;58:E007.

72. Wang XF, Yuan J, Zheng YJ, Chen J, Bao YM, Wang YR, et al. [Clinical and epidemiological characteristics of 34 children with 2019 novel coronavirus infection in Shenzhen]. Zhonghua Er Ke Za Zhi. 2020;58:E008.
Figure 1. Study selection and characteristics.

PRISMA 2009 Flow Diagram

Records identified through PubMed database searching (n = 450)

Additional records identified through Scopus database searching (n = 185)

Additional records identified through Web of Sciences database searching (n = 25)

Records after duplicates removed (n = 67)

Records screened (n = 67)

Full-text articles assessed for eligibility (n = 64)

Studies included in qualitative synthesis (n = 58)

Studies included in quantitative synthesis (meta-analysis) (n = 19)

Records excluded due to lack of information on molecular diagnosis (n = 3)

Full-text articles excluded due to lack of information on molecular diagnosis (n = 6)

Case reports, descriptive summary analysis (n = 39)
Table 1. Characteristics of the included studies on COVID-19, 2020. All patients confirmed by real-time RT-PCR.

| Author                     | Journal               | Date (MM/DD) | Country | Study type         | N  | Quality score* | Reference |
|----------------------------|-----------------------|--------------|---------|-------------------|----|----------------|-----------|
| WMCHHHPNCI Wuhan Munic...   | Comission Report      | 01/20 China  |         | Cross-sectional   | 136| 12             | [59]      |
| Chaolin et al.             | Lancet                | 01/24 China  |         | Cross-sectional   | 41 | 19             | [4]       |
| Li et al.                  | NEJM                  | 01/29 China  |         | Cross-sectional   | 425| 19             | [10]      |
| Chen et al.                | Lancet                | 01/30 China  |         | Cross-sectional   | 99 | 19             | [3]       |
| Chung et al.               | Radiology             | 02/04 China  |         | Cross-sectional   | 21 | 12             | [60]      |
| Chen et al.                | Chin J Tuberc Respir Dis | 02/06 China |         | Cross-sectional   | 29 | 12             | [61]      |
| Wang et al.                | JAMA                  | 02/07 China  |         | Cross-sectional   | 138| 19             | [62]      |
| Kui et al.                 | Chin Med J            | 02/07 China  |         | Cross-sectional   | 137| 12             | [63]      |
| Chang et al.               | JAMA                  | 02/07 China  |         | Cross-sectional   | 13 | 14             | [64]      |
| To et al.                  | Clin Infect Dis       | 02/12 China  |         | Cross-sectional   | 12 | 14             | [65]      |
| COVID-19 team Australia    | Team Report           | 02/12 Australia |       | Cross-sectional   | 15 | 12             | [66]      |
| Yueying et al.             | Eur Radiol            | 02/13 China  |         | Cross-sectional   | 63 | 14             | [67]      |
| Li et al.                  | Preprint Lancet       | 02/13 China  |         | Case series       | 24 | 14             | [68]      |
| Feng et al.                | Radiology             | 02/13 China  |         | Case series       | 21 | 12             | [69]      |
| Liang et al.               | Lancet Oncology       | 02/14 China  |         | Cross-sectional   | 1590| 17            | [37]      |
| Zhang et al.               | Chin J Tuberc Respir Dis | 02/15 China |         | Case series       | 9  | 12             | [36]      |
| Feng et al.                | Chin J Pediatr        | 02/17 China  |         | Case series       | 15 | 12             | [70]      |
| Wang et al.                | Chin J Pediatr        | 02/17 China  |         | Cross-sectional   | 34 | 12             | [71]      |
| Xiaobo et al.              | Lancet Respir Med     | 02/21 China  |         | Cross-sectional   | 52 | 17             | [48]      |
Table 2. Demographical characteristics, ICU, and comorbidities of the study subjects.

| Author                             | Date (MM/DD) | N  | Mean Age (y-old) | Age Range | Sex (Male) | N at ICU | Comorbidities | Diabetes | Hypertension | Cardiovascular disease | Chronic obstructive pulmonary disease | Malignancies | Chronic liver disease | Reference |
|------------------------------------|--------------|----|------------------|-----------|------------|----------|--------------|----------|--------------|------------------------------|----------------------------------------|--------------|-----------------------|-----------|
| WMCHHPNICI                         | 01/20        | 136| -                | 25-89     | 66         | -        | -            | -        | -            | 6 (14.6)                     | 6 (14.6)                              | -            | -                     | [59]      |
| Chaolin et al.                     | 01/24        | 41 | 49               | 41-58     | 30         | 13 (31.7)| 13 (31.7)    | 8 (19.5) | 6 (14.6)     | 1 (2.4)                     | 1 (2.4)                               | -            | -                     | [4]       |
| Li et al.                          | 01/29        | 425| 56               | 26-82     | 240        | -        | -            | -        | -            | -                           | -                                      | -            | -                     | [10]      |
| Chen et al.                        | 01/30        | 99 | 55.5             | 21-82     | 67         | 23 (23.2)| 50 (50.5)    | 12 (12.1)| -            | -                           | 40 (40.4)                             | 1 (1.0)    | 1 (1.0)               | [3]       |
| Chung et al.                       | 02/04        | 21 | 51               | 29-77     | 13         | -        | -            | -        | -            | 8 (27.6)                    | -                                      | -            | -                     | [60]      |
| Chen et al.                        | 02/06        | 29 | 56               | 26-79     | 21         | -        | 16 (55.2)    | 5 (17.2) | 8 (27.6)     | -                           | -                                      | -            | 1 (3.4)               | [61]      |
| Wang et al.                        | 02/07        | 138| 56               | 42-68     | 75         | 36 (26.1)| 64 (46.4)    | 14 (10.1)| 43 (31.2)    | 20 (14.5)                   | 4 (2.9)                               | 10 (7.2)    | 4 (2.9)               | [62]      |
| Kui et al.                         | 02/07        | 137| 57               | 20-83     | 61         | -        | 27 (19.7)    | 14 (10.2)| 13 (9.5)     | 10 (7.3)                    | 2 (1.5)                               | 2 (1.5)     | -                     | [63]      |
| Chang et al.                       | 02/07        | 13 | 34               | 34-48     | 10         | -        | -            | -        | -            | -                           | -                                      | -            | -                     | [64]      |
| To et al.                          | 02/12        | 12 | 62.5             | 37-75     | 7          | -        | -            | -        | -            | -                           | -                                      | -            | -                     | [65]      |
| COVID-19 team Australia            | 02/12        | 15 | 43               | 8-66      | 9          | 1 (6.7)  | -            | -        | -            | -                           | -                                      | -            | -                     | [66]      |
| Yuying et al.                      | 02/13        | 63 | -                | 15.2-44.9 | 33         | -        | -            | -        | -            | -                           | -                                      | -            | -                     | [67]      |
| Li et al.                          | 02/13        | 24 | 43               | 12-84     | 8          | -        | -            | -        | -            | -                           | -                                      | -            | -                     | [68]      |
| Feng et al.                        | 02/13        | 21 | 40.9             | 25-63     | 6          | -        | -            | -        | -            | -                           | -                                      | -            | -                     | [69]      |
| Liang et al.                       | 02/14        | 1590| -               | 911       | 130 (8.2)| 18 (1.1)| 2 (0.1)     | 2 (0.1) | 1 (0.06)    | -                           | -                                      | -            | -                     | [37]      |
| Zhang et al.                       | 02/15        | 9  | 36               | 15-49     | 5          | -        | 1 (11.1)    | 1 (11.1)| -            | -                           | -                                      | -            | -                     | [36]      |
| Feng et al.                        | 02/17        | 15 | -                | 4-14      | 5          | -        | -            | -        | -            | -                           | -                                      | -            | -                     | [70]      |
| Wang et al.                        | 02/17        | 34 | 8                | -         | 14         | -        | -            | -        | -            | -                           | -                                      | -            | -                     | [71]      |
| Xiaobo et al.                      | 02/21        | 52 | 59.7             | 33.6-85.8 | 35         | -        | 21 (40.4)   | 9 (17.3)| 5 (9.6)     | 4 (7.7)                     | 2 (3.8)                               | -            | -                     | [48]      |

WMCHHPNICI, Wuhan Municipal Commission of Health and Health on Pneumonia of New Coronavirus Infection. MM/DD, Month, Day. ICU, intensive care unit. y-old, years old.
### Table 3. Clinical characteristics of the study subjects.

| Author                      | Date (MM/DD) | N     | Fever (N, %) | Cough (N, %) | Sore Throat (N, %) | Myalgia or fatigue (N, %) | Sputum production (N, %) | Headache (N, %) | Haemoptisis (N, %) | Diarrhoea (N, %) | Dyspnoea (N, %) | Reference |
|-----------------------------|--------------|-------|--------------|--------------|--------------------|--------------------------|--------------------------|----------------|-------------------|----------------|----------------|-----------|
| WMCHHHIPNCI                 | 01/20        | 136   | 136 (100.0)  | 136 (100.0)  | -                  | -                        | -                        | -              | -                 | -              | -              | [59]      |
| Chaolin et al.              | 01/24        | 41    | 40 (97.6)    | 31 (75.6)    | 0 (0.0)            | 18 (43.9)                | 11 (26.8)                | 3 (7.3)        | 2 (4.9)           | 1 (2.4)        | 22 (53.7)      | [4]       |
| Li et al.                   | 01/29        | 425   | -            | -            | -                  | -                        | -                        | -              | -                 | -              | -              | [10]      |
| Chen et al.                 | 01/30        | 99    | 82 (82.8)    | 81 (81.8)    | 5 (5.1)            | 11 (11.1)                | -                        | 8 (8.1)        | -                 | 2 (2.0)        | 31 (31.3)      | [3]       |
| Chang et al.                | 02/04        | 21    | 14 (66.7)    | 9 (42.9)     | -                  | 6 (28.6)                 | -                        | 3 (14.3)       | -                 | -              | -              | [60]      |
| Chen et al.                 | 02/06        | 29    | 28 (96.6)    | 21 (72.4)    | -                  | 12 (41.4)                | 21 (72.4)                | 2 (6.9)        | -                 | 4 (13.8)       | 17 (58.6)      | [61]      |
| Wang et al.                 | 02/07        | 138   | 136 (98.6)   | 82 (59.4)    | 24 (17.4)          | 138 (100.0)              | 37 (26.8)                | 9 (6.5)        | -                 | 14 (10.1)      | 43 (31.2)      | [62]      |
| Kui et al.                  | 02/07        | 137   | 112 (81.8)   | 66 (48.2)    | -                  | 44 (32.1)                | 6 (4.4)                  | 13 (9.5)       | 7 (5.1)           | 11 (8.0)       | 26 (19.0)      | [63]      |
| Chang et al.                | 02/07        | 13    | 12 (92.3)    | 6 (46.2)     | -                  | 3 (23.1)                 | 2 (15.4)                 | 3 (23.1)       | -                 | 1 (7.7)        | -              | [64]      |
| To et al.                   | 02/12        | 12    | -            | -            | -                  | -                        | -                        | -              | -                 | -              | -              | [65]      |
| COVID-19 team Australia     | 02/12        | 15    | 14 (93.3)    | 11 (73.3)    | -                  | -                        | -                        | -              | -                 | -              | -              | [66]      |
| Yueying et al.              | 02/13        | 63    | -            | -            | -                  | -                        | -                        | -              | -                 | -              | -              | [67]      |
| Li et al.                   | 02/13        | 24    | 19 (79.2)    | 6 (25.0)     | -                  | 6 (25.0)                 | -                        | 4 (16.7)       | -                 | 2 (8.3)        | -              | [68]      |
| Feng et al.                 | 02/13        | 21    | 18 (85.7)    | 12 (57.1)    | 4 (19.0)           | 11 (52.4)                | 6 (28.6)                 | -              | -                 | -              | -              | [69]      |
| Liang et al.                | 02/14        | 1590  | -            | -            | -                  | -                        | -                        | -              | -                 | -              | -              | [37]      |
| Zhang et al.                | 02/15        | 9     | 8 (88.9)     | 5 (55.6)     | 4 (44.4)           | 4 (44.4)                 | -                        | -              | -                 | -              | -              | [36]      |
| Feng et al.                 | 02/17        | 15    | 5 (33.3)     | 1 (6.7)      | -                  | -                        | -                        | -              | -                 | -              | -              | [70]      |
| Wang et al.                 | 02/17        | 34    | 17 (50.0)    | 13 (38.2)    | -                  | -                        | -                        | -              | -                 | -              | -              | [71]      |
| Xiaobo et al.               | 02/21        | 52    | 51 (98.1)    | 40 (76.9)    | -                  | 6 (76.9)                 | 3 (11.5)                 | -              | -                 | 33 (63.5)      | -              | [48]      |

WMCHHHIPNCI, Wuhan Municipal Commission of Health and Health on Pneumonia of New Coronavirus Infection. MM/DD, Month, Day.
Table 4. Laboratory characteristics of the study subjects.

| Author           | Date (MM/DD) | N  | Leucocytosis | Leukopenia | Lymphopenia | High AST | High Creatinine | High Creatine kinase | High LDH | High Troponin I, >99th perc | Anemia | Decreased Albumin | High ALT | High Bilirubin | Erythrocyte sedimentation rate elevated | C-reactive protein, high | Serum ferritin | Reference |
|------------------|--------------|----|--------------|------------|-------------|----------|-----------------|----------------------|----------|--------------------------|--------|---------------------|---------|---------------|--------------------------------|--------------------------|----------------|-----------|
| WMCHHHHPNCI      | 01/20        | 136| -            | -          | -           | -        | -               | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [59]      |
| Chaolin et al.   | 01/24        | 41 | 12 (29.3)    | 10 (24.4)  | 26 (63.4)   | 15 (36.6)| 4 (9.8)         | 13 (31.7)            | 29 (70.7) | 5 (12.2)                 | -      | -                   | -       | -             | -                                 | -                        | -             | [4]       |
| Li et al.        | 01/29        | 425| -            | -          | -           | -        | -               | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [10]      |
| Chen et al.      | 01/30        | 99 | 24 (24.2)    | 9 (9.1)    | 35 (35.4)   | 35 (35.4)| 3 (3.0)         | 13 (13.1)            | 75 (75.8) | 50 (50.5)                | 97 (98.0)| 28 (28.3)          | 18 (18.2)| 84 (84.8)     | 63 (63.6)                        | 62 (62.6)                | [3]          |
| Chuang et al.    | 02/04        | 21 | -            | -          | -           | -        | -               | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [60]      |
| Chen et al.      | 02/06        | 29 | 6 (20.7)     | 6 (20.7)   | 20 (69.0)   | 7 (24.1) | 2 (6.9)         | 20 (69.0)            | -        | 15 (51.7)                | 5 (17.2)| 1 (3.4)             | -       | 27 (93.1)     | -                                 | -                        | -             | [61]      |
| Wang et al.      | 02/07        | 138| 0 (0.0)      | 0 (0.0)    | 97 (70.3)   | -        | 55 (39.9)       | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [62]      |
| Kui et al.       | 02/07        | 137| 26 (19.0)    | 51 (37.2)  | 99 (72.3)   | -        | -               | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [63]      |
| Chang et al.     | 02/07        | 13 | -            | -          | -           | -        | -               | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [64]      |
| To et al.        | 02/12        | 12 | -            | -          | -           | -        | -               | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [65]      |
| COVID-19 team    |              |    |              |            |             | -        | -               | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [66]      |
| Yueying et al.   | 02/13        | 63 | -            | -          | -           | -        | -               | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [67]      |
| Li et al.        | 02/13        | 24 | 5 (20.8)     | 2 (8.3)    | -           | -        | -               | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [68]      |
| Feng et al.      | 02/13        | 21 | -            | -          | -           | -        | -               | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [69]      |
| Liang et al.     | 02/14        | 1590| -             | -          | -           | -        | -               | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [37]      |
| Zhang et al.     | 02/15        | 9  | 1 (11.1)     | 2 (22.2)   | -           | -        | -               | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [36]      |
| Feng et al.      | 02/17        | 15 | -            | 8 (53.3)   | -           | -        | -               | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [70]      |
| Wang et al.      | 02/17        | 34 | 5 (14.7)     | 1 (2.9)    | 1 (2.9)     | 1 (2.9)  | 10 (29.4)       | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [71]      |
| Xuebo et al.     | 02/21        | 52 | -            | -          | -           | -        | -               | -                    | -        | -                        | -      | -                   | -       | -             | -                                 | -                        | -             | [48]      |
Table 5. Imaging and complications of the study subjects.

| Author                  | Date (MM/DD) | N   | Chest Ray Unilateral Pneumonia | Chest Ray Bilateral Pneumonia | Ground-glass opacity | Acute respiratory distress syndrome | RNAemia | Acute cardiovascular injury | Acute kidney injury | Secondary infection | Shock | Hospitalization | Discharge | Death | Reference |
|-------------------------|--------------|-----|--------------------------------|--------------------------------|----------------------|-------------------------------------|----------|---------------------------|-------------------|---------------------|--------|-----------------|-----------|-------|-----------|
| WMCHHHHPNCI             | 01/20        | 136 | -                              | -                              | -                    | -                                  | -        | -                         | -                 | -                   | -      | -               | -         | -     | [59]      |
| Chaulin et al.          | 01/24        | 41  | -                              | 40 (97.6)                       | -                    | -                                  | 425 (100.0) | -                         | -                 | -                   | -      | -               | -         | -     | [4]       |
| Li et al.               | 01/29        | 425 | -                              | -                              | -                    | 425 (100.0)                       | -        | -                         | -                 | -                   | -      | -               | -         | -     | [10]      |
| Chen et al.             | 01/30        | 99  | 25 (25.3)                      | 74 (74.7)                       | 14 (14.1)            | 17 (17.2)                         | 99 (100.0) | -                         | 3 (3.0)           | 4 (4.0)             | 57 (57.6) | 31 (31.3)      | 11 (11.1) | -     | [3]       |
| Chung et al.            | 02/04        | 21  | 2 (1.5)                        | 16 (11.8)                       | 18 (13.2)            | -                                  | 21 (15.4) | -                         | -                 | -                   | 21 (15.4) | -               | -         | -     | [60]      |
| Chen et al.             | 02/06        | 29  | -                              | 29 (100.0)                      | -                    | 29 (100.0)                        | -        | -                         | -                 | -                   | 27 (93.1) | -               | 2 (6.9)   | -     | [61]      |
| Wang et al.             | 02/07        | 138 | 0 (0.0)                        | 138 (100.0)                     | 138 (100.0)          | 27 (19.6)                         | 138 (100.0) | 10 (7.2)                  | 5 (3.6)           | 12 (8.7)            | 138 (100.0) | 47 (34.1)      | 6 (4.3)    |       | [62]      |
| Kui et al.              | 02/07        | 137 | -                              | 36 (26.3)                       | 55 (40.1)            | -                                  | 137 (100.0) | -                         | -                 | -                   | 77 (56.6) | 44 (32.4)      | 16 (11.8) |       | [63]      |
| Chang et al.            | 02/07        | 13  | 1 (7.7)                        | -                              | 6 (46.2)             | -                                  | 13 (100.0) | -                         | -                 | -                   | 12 (92.3) | 1 (7.7)        | -         | -     | [64]      |
| To et al.               | 02/12        | 12  | -                              | -                              | -                    | 12 (100.0)                        | -        | -                         | -                 | -                   | 12 (100.0) | -               | -         | -     | [65]      |
| COVID-19 team Australia | 02/12        | 15  | -                              | -                              | -                    | 15 (100.0)                        | -        | -                         | -                 | -                   | 11 (73.3) | -               | -         | -     | [66]      |
| Yueying et al.          | 02/13        | 63  | -                              | 38 (60.3)                      | 14 (22.2)            | -                                  | 63 (100.0) | -                         | -                 | -                   | -      | -               | -         | -     | [67]      |
| Li et al.               | 02/13        | 24  | -                              | -                              | -                    | 24 (100.0)                        | -        | -                         | -                 | -                   | -      | -               | -         | -     | [68]      |
| Feng et al.             | 02/13        | 21  | 18 (85.7)                      | -                              | -                    | 21 (100.0)                        | -        | -                         | -                 | -                   | 21 (100.0) | -               | -         | -     | [69]      |
| Liang et al.            | 02/14        | 1590| -                              | -                              | -                    | 1590 (100.0)                     | -        | -                         | -                 | -                   | -      | -               | -         | -     | [37]      |
| Zhang et al.            | 02/15        | 9   | 2 (22.2)                       | 5 (55.6)                       | 7 (77.8)             | 9 (100.0)                         | -        | -                         | -                 | -                   | 9 (100.0) | -               | -         | -     | [36]      |
| Feng et al.             | 02/17        | 15  | 4 (26.7)                       | 8 (53.3)                       | -                    | 15 (100.0)                        | -        | -                         | -                 | -                   | 15 (100.0) | -               | -         | -     | [70]      |
| Wang et al.             | 02/17        | 34  | -                              | 34 (100.0)                     | -                    | 34 (100.0)                        | -        | -                         | -                 | -                   | 34 (100.0) | 34 (100.0)     | -         | -     | [71]      |
| XiaoBo et al.           | 02/21        | 52  | -                              | -                              | 35 (67.3)            | -                                  | 12 (23.1) | 15 (28.8)                 | 2 (3.8)           | 52 (100.0)          | -      | 32 (61.5)      | -         | -     | [48]      |
Table 6. Meta-analysis outcomes (random-effects model)².

| Variable                                      | Number of Studies | Mean (y-old) / Prevalence (%) | 95% CI | n       | I²      | t²      | p     |
|-----------------------------------------------|-------------------|--------------------------------|--------|---------|---------|---------|-------|
| Age                                           | 18                | 51.97                          | 46.06-57.89 | 2626   | 1193.28 | 98.56   | 0.001 |
| Male                                          | 22                | 55.9                           | 51.6-60.1 | 2874   | 61.98   | 66.12   | 0.005 |
| ICU                                           | 6                 | 20.3                           | 10.0-30.6 | 1883   | 49.49   | 89.89   | 0.013 |
| Comorbidities                                 | 7                 | 36.8                           | 24.7-48.9 | 505    | 47.75   | 87.44   | <0.001|
| Hypertension                                  | 5                 | 18.6                           | 8.1-29.0  | 363    | 23.98   | 83.33   | <0.001|
| Cardiovascular disease                        | 6                 | 14.4                           | 5.7-23.1  | 485    | 45.29   | 88.96   | <0.001|
| Diabetes                                      | 8                 | 11.9                           | 9.1-14.6  | 523    | 4.065   | 1.00    | 0.772 |
| Chronic obstructive pulmonary disease         | 6                 | 1.8                            | 0.6-3.0   | 485    | 4.413   | 1.00    | 0.492 |
| Malignancies                                  | 6                 | 2.5                            | 0.7-4.2   | 496    | 7.39    | 1.00    | 0.180 |
| Chronic liver disease                         | 3                 | 3.0                            | 0.7-5.4   | 208    | 0.744   | 0.00    | 0.689 |

Clinical manifestations

- Fever: 15 studies, 88.7% (84.5-92.9) n=784, 89.12, p<0.001
- Adult: 13 studies, 92.8% (89.4-96.2) n=735, 82.42, p<0.001
- Children: 2 studies, 43.9% (28.2-59.6) n=49, 20.2, p=0.003
- Cough: 15 studies, 57.6% (40.8-74.4) n=784, 97.87, p<0.001
- Adult: 13 studies, 63.4% (48.0-78.8) n=735, 97.09, p<0.001
- Children: 2 studies, 22.0% (0.0-52.9) n=49, 88.87, p=0.044
- Dyspnea: 8 studies, 45.6% (10.9-80.4) n=656, 99.48, p=0.248
- Myalgia or fatigue: 11 studies, 29.4% (19.3-39.0) n=446, 80.66, p<0.001
- Sputum production: 6 studies, 28.5% (10.8-46.3) n=379, 94.73, p=0.044
- Sore throat: 5 studies, 11.0% (2.8-19.2) n=308, 85.39, p=0.006
- Headache: 9 studies, 8.0% (5.7-10.2) n=554, 0.00, p=0.052
- Dizniha: 6 studies, 6.1% (2.4-9.7) n=457, 61.21, p=0.022

Laboratory findings

- Decreased Albumin: 2 studies, 75.8% (30.5-100.0) n=128, 95.88, p=0.103
- High C-reactive protein: 6 studies, 58.3% (21.8-94.7) n=332, 98.94, p=0.200
- High LDH: 5 studies, 57.0% (38.0-76.0) n=341, 92.59, p=0.043
- Lympohpenia: 8 studies, 43.1% (18.9-67.3) n=511, 97.99, p=0.117
- High Erythrocyte sedimentation rate: 3 studies, 41.8% (0.0-92.8) n=157, 98.31, p=0.199
- High AST: 3 studies, 33.3% (26.3-40.4) n=169, 1.7, p=0.00, p=0.047
- High ALT: 2 studies, 24.1% (13.5-34.6) n=128, 42.84, p=0.003
- High Creatinine Kinase: 2 studies, 21.3% (3.2-39.4) n=140, 93.36, p=0.004
- Leukopenia: 8 studies, 18.7% (8.5-28.8) n=517, 94.48, p=0.018
- Leukocytosis: 7 studies, 16.8% (5.5-28.0) n=487, 93.14, p=0.019
- High Bilirubin: 2 studies, 10.7% (0.0-25.1) n=128, 87.79, p=0.004
- High Creatinine: 3 studies, 4.5% (1.0-8.0) n=169, 10.17, p=0.328

Chest X-Ray Pneumonia Compromise

- Unilateral: 7 studies, 25.0% (5.2-44.8) n=316, 96.37, p=0.005
- Bilateral: 9 studies, 72.9% (58.6-87.1) n=557, 98.28, p=0.042
- Adult: 7 studies, 70.7% (50.9-91.0) n=508, 95.87, p=0.070
- Children: 2 studies, 77.7% (33.5-100.0) n=49, 91.69, p=0.094

Image findings

- Ground-glass opacity: 10 studies, 68.5% (51.8-85.2) n=584, 99.09, p=0.006

Complications

- RAemia: 18 studies, 96.8% (94.9-98.7) n=1096, 92.95, p=0.001
- Adult: 16 studies, 96.6% (94.6-98.6) n=1047, 93.77, p=0.001
- Children: 2 studies, 98.3% (94.7-100.0) n=49, 0.125, p=0.00, p=0.073
- Acute respiratory distress syndrome: 4 studies, 32.8% (13.7-51.8) n=330, 93.93, p=0.035
- Acute cardiac injury: 3 studies, 13.0% (4.1-21.9) n=231, 70.22, p=0.004
- Acute kidney injury: 4 studies, 7.9% (1.8-14.0) n=330, 81.85, p=0.003
- Shock: 3 studies, 6.2% (3.1-9.3) n=278, 14.67, p=0.030
- Secondary infections: 2 studies, 5.6% (0.3-10.9) n=93, 18.16, p=0.026
- Hospitalization: 15 studies, 87.9% (84.2-91.6) n=2211, 96.42, p=0.001

Outcome

- Discharged: 7 studies, 52.9% (23.9-81.8) n=477, 98.77, p=0.15
- Death: 7 studies, 13.9% (6.2-21.5) n=632, 91.4, p=0.009

*95% CI = 95% confidence interval. ICU, intensive care unit. y-old, years old. AST, Aspartate transaminase. ALT, Alanine transaminase.
† Crohcan’s Q statistic for heterogeneity.
‡ I² index for the degree of heterogeneity.
§ Tau-squared measure of heterogeneity.
Table 7. Summary of the case report findings.\(^8\)

| Variables                                      | N (126) | %  | Variables                                      | N (126) | %  |
|------------------------------------------------|---------|----|------------------------------------------------|---------|----|
| Age (y-old) (mean, SD) (n=118)                 | 47.9    | 22.2 | Images                                         |         |    |
| Sex (Male/Female) (n=71)                       | 49      | 69.01 | Ground-glass opacity at chest X-ray            | 58      | 46.0 |
| ICU (Yes)                                       | 11      | 8.7  | Chest X-Ray Bilateral Pneumonia               | 50      | 39.7 |
| Comorbidities                                   | 13      | 10.3 | Chest X-Ray Unilateral Pneumonia              |         |    |
| Hypertension                                    | 13      | 10.3 | Complications                                  |         |    |
| Chronic liver disease                          | 5       | 4.0  | RNAemia                                        |         |    |
| Cardiovascular disease                         | 3       | 2.4  | Acute respiratory distress syndrome           | 9       | 7.1  |
| Chronic obstructive pulmonary disease           | 2       | 1.6  | Secondary infection                            | 2       | 1.6  |
| Malignancy or cancer                            | 1       | 0.8  | Acute kidney injury                            | 1       | 0.8  |
| Clinical features                               |         |      | Shock                                          | 1       | 0.8  |
| Fever                                          | 97      | 77.0 | Hospitalization                                |         |    |
| Cough                                          | 70      | 55.6 | Outcomes                                       |         |    |
| Myalgia or fatigue                             | 39      | 31.0 | Discharge                                      |         |    |
| Dyspnoea                                        | 27      | 21.4 | Death                                          | 20      | 15.9 |
| Sputum production                               | 16      | 12.7 | Countries of the case report articles (39)     |         |    |
| Sore Throat                                     | 13      | 10.3 | China                                          | 25      | 64.1 |
| Diarrhoea                                       | 8       | 6.3  | South Korea                                    | 4       | 10.3 |
| Headache                                       | 7       | 5.6  | Australia                                      | 1       | 2.6  |
| Haemoptisis                                     | 1       | 0.8  | Canada                                         | 1       | 2.6  |
| Laboratory findings                            |         |      | France                                         | 1       | 2.6  |
| Lymphopenia                                     | 30      | 23.8 | Germany                                        | 1       | 2.6  |
| High C-reactive protein                         | 28      | 22.2 | Japan                                          | 1       | 2.6  |
| High AST                                        | 10      | 7.9  | Nepal                                          | 1       | 2.6  |
| Leukopenia                                      | 9       | 7.1  | Taiwan                                         | 1       | 2.6  |
| High ALT                                        | 9       | 7.1  | Thailand                                       | 1       | 2.6  |
| High LDH                                        | 8       | 6.3  | United States of America                       | 1       | 2.6  |
| High Erythrocyte sedimentation rate             | 6       | 4.8  | Vietnam                                        | 1       | 2.6  |
| Leucocytosis                                    | 4       | 3.2  | Countries of the cases reported (n=126)        |         |    |
| Anemia                                          | 4       | 3.2  | China                                          | 101     | 80.2 |
| Decreased Albumin                              | 3       | 2.4  | South Korea                                    | 6       | 4.8  |
| High Creatinine                                | 2       | 1.6  | Germany                                        | 5       | 4.0  |
| High Creatine kinase                           | 2       | 1.6  | France                                         | 3       | 2.4  |
| High Bilirubin                                  | 1       | 0.8  | Australia                                      | 2       | 1.6  |
|                                                   |         |      | Taiwan                                         | 2       | 1.6  |
|                                                   |         |      | Vietnam                                        | 2       | 1.6  |
|                                                   |         |      | Canada                                         | 1       | 0.8  |
|                                                   |         |      | Japan                                          | 1       | 0.8  |
|                                                   |         |      | Nepal                                          | 1       | 0.8  |
|                                                   |         |      | Thailand                                       | 1       | 0.8  |
|                                                   |         |      | United States of America                       | 1       | 0.8  |

\(^8\)The list of case reports is available at Table S1—supplemental materials.
Supplemental Materials.

**Figure S1.** Funnel-plot for the Standard Error by Logit Event rate to assess for publication bias.
Figure S2. Pool prevalences forest plots of findings described in Table 2.
| Table S1. Case reports included in the review. |
|---------------------------------------------|
| **Article title** | **List of authors** | **Journal name** | **Year** | **PMID** | **doi** |
| Emergence of a novel coronavirus causing respiratory illness in Wuhan, China | Julian W. Tang, Paul A. Tambyah, David S.C. Hui | Journal of Infection | 2020 | 02006 | 10.1016/j.jinf.2020.01.014 |
| Public responses to the novel 2019 coronavirus in Japan: mental health consequences and target populations | Jun Shimamura, Robert J. Uoma, Joshua C. Morganstein, Mire Kuroswa, David M. Benedek | Psychiatry and Clinical Neurosciences | 2020 | 02049 | 10.1111/pcn.12988 |
| Clinical characteristics and therapeutic procedure for four cases with 2019 novel coronavirus pneumonia receiving combined Chinese and Western medicine treatment | Zhexue Wang, Xiaorong Chen, Yunfei Lu, Førtei Chen, Wei Zhang | Biorxiv Trends | 2020 | 02049 | 10.5822/bio.2020.01030 |
| A locally transmitted case of SARS-CoV-2 infection in Taiwan | Ying-Chu Liu, Ching-Hua Liao, Chen-Fu Chang, Cha-Chung Chou, Yan-Ren Lin | The New England Journal of Medicine | 2020 | 02012 | 10.1056/NEJMoa2001573 |
| Journey of a Thai Taxi Driver and Novel Coronavirus | Wannarat A. Pongpirul, Krit Pongpirul, Anuttra C. Chamnongthai, Wutthi Prasitsukthai. | The New England Journal of Medicine | 2020 | 02013 | 10.1056/NEJMoa2001468 |
| Clinical characteristics and intratracheal vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records | Hunqin Chen, Junjuan Guo, Chen Wang, Fan Luo, Naiqichen Yu, Wei Zhang, Jiafu Li, Dongshi Zhao, Dan Xu, Qing Gong, Jing Liao, Huijia Yang, Wei Hou, Yuanshen Chang | The Lancet | 2020 | 02012 | 10.1016/S0140-6736(20)30660-3 |
| Identification of a novel coronavirus causing severe pneumonia in human: a descriptive study | Ren LL, Wang YM, Wu ZQ, Xiang ZC, Guo L, Xu X, Tang YZ, Xiong Y, Li YL, Li XY, Li H, Fan GEH, Gu XY, Xiao Y, Guo H, Xu XY, Yang F, Wang XM, Wu C, Chen L, Lin YW, Liu B, Yang J, Wang XR, Dong J, Li L, Huang CL, Zhao JF, Hu Y, Yang JS, Liu LL, Zhan QH, Qin J, Cao B. | Chinese Medical Journal | 2020 | 02011 | 10.1097/CM9.000000000000722 |
| Novel Coronavirus Infection in Hospitalized Infants Under 1 Year of Age in China: Case of the Index Patient Who Caused Tertiary Transmission of Coronavirus Disease 2019 in Korea: the Application of Laparoscopy/Renover to the Treatment of COVID-19 Pneumonia Monitored by Quantitative RT-PCR | Min Wei, Jinping Yuan, MD, Yu Liu, Tao Fu, Xue Yu, Zhi-Juan Zhang. | JAMA | 2020 | 02014 | 10.1001/jama.2020.2131 |
| Novel Coronavirus Pneumonia Outbreak in 2019: Computed Tomographic Findings in Two Cases | Xiaogu Liu, Zhenyu Gong, Zake Xiao, Jingfang Xiong, Bing Fan, Saiq Liu | Journal of Korean medical science | 2020 | 02017 | 10.3346/jkms.2020.35.e79 |
| Novel Coronavirus Pneumonia Imaging of the 2019 Novel Coronavirus Case of the Index Patient Who Caused Tertiary Transmission of Coronavirus Disease 2019: Descriptive Study | Junjiang Lei, Junfeng Li, Xian Li, Xue-long Qi. | Radiology - Radiological Society of North America | 2020 | 01031 | doi.org/10.1148/radiol.2020200236 |
| First imported case of 2019 novel coronavirus in Canada, presenting as mild pneumonia | William Kyle Silverstein, Lynfa Stroud, Graham Edward Cleghorn, Jerome Allen Leis | The Lancet | 2020 | 02013 | 10.1016/S0140-6736(20)30706-0 |
| Imaging features of novel coronavirus pneumonia | Xi Xu, Chengcheng Yu, Lieqiang Zhang, Lianggeng Luo, Junxun Liu | European Journal of Nuclear Medicine and Molecular Imaging | 2020 | 02014 | 10.1007/s00259-020-04720-2 |
| Importation and Human-to-Human Transmission of a Novel Coronavirus in Vietnam | Phu NT, Nguyen TV, Loang QC, Nguyen TV, Nguyen HT, Le HQ, Nguyen TT, Cao TM, Pham QD | The New England Journal of Medicine | 2020 | 01028 | 10.1056/NEJMc2001272 |
| 2019 Novel Coronavirus (2019-nCoV) Pneumonia | Peng Liu, Xian-cheng Tan. | Radiology - Radiological Society of North America | 2020 | 02040 | doi.org/10.1148/radiol.2020200257 |
| A new coronavirus associated with human respiratory disease in China | Fan Wu, Su Zhao, Bin Yu, Yan-Mei Chen, Wen Wang, Zhi-Gang Song, Yi Hu, Zhao-Wu Tao, Junhua Tian, Yuan-Yuan Pei, Minge Li Yuan, Yu-Lung Zhang, Fa-Hui Dai, Yi Liu, Qi-Min Wang, Jiao-Hao Zheng, Lin Na, Edward C. Holmes & Yong-Zhen Zhang | Nature | 2020 | 02043 | 10.1038/s41586-020-0663-8 |
| A pneumonia outbreak associated with a new coronavirus of probable bat origin | Peng Zhou, Xing-Lou Yang, Xian-Guang Wang, Ben Hu, Li Zhang, Wei Zhang, Hao-Rui Si, Yan Zhai, Bi Li, Chao-Lun Huang, Huan-Dong Chen, Jing Chen, Yan Liu, Hua Guo, Ren-Di Jiang, Mei-Qin Liu, Ying Chen, Xu-Rui Shi, Xin Wang, Xiao-Shuang Zhong, Kai Zhao, Quan-Jiao Chen, Fei Deng, Lin-Liu Liu, Bing Yan, Fan Xian-Zhan, Yan-Yi Wang, Geng-Fu Xiao & Zheng Li Shu. | Nature | 2020 | 02043 | 10.1038/s41586-020-0621-7 |
| A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster | Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, Xing F, Liu J, Ying CC, Poon RW, Tox HW, Lo SK, Chan KH, Poon VK, Chan WM, Ip JD, Cai JP, Cheng VC, Chen H, Hui CK, Yuen KY. | The Lancet | 2020 | 01024 | 10.1016/S0140-6736(20)30514-9 |
| First case of 2019 novel coronavirus infection in children in Shanghai | Cui H, Wang XS, Gu YL, Xiao AM, Chang HL, Tan H, Zhu YX, Wang QR, Zeng JY. | Chinese journal of pediatrics | 2020 | 02044 | 10.3760/cma.j.issn.0021-1310.2020.00022 |
| A Novel Coronavirus From Patients With Pneumonia in China, 2019 | Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Nie P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W | The New England Journal of Medicine | 2020 | 01024 | 10.1056/NEJMoa2001017 |
| Article title                                                                 | List of authors                              | Journal name                                      | Year | MMD P | doi          |
|------------------------------------------------------------------------------|----------------------------------------------|---------------------------------------------------|------|-------|--------------|
| Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China | Wang W, Tang J, Wei F                         | Journal of medical virology                      | 2020 | 01/29 | 10.1002/jmv.25689 |
| Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany | Rothe C1, Schunk M, Sottmann P, Bertzig G, Froschel G, Wallrauch C, Zimmer T, Thiel V, Janke C, Gaggenau W, Stitmayer M, Drosten C, Vollmar P, Zwieglmaier K, Zange S, Wolff R, Hoelscher M | The New England Journal of Medicine               | 2020 | 01/30 | 10.1056/NEJMc2001468 |
| COVID-19, Australia: Epidemiology Report 2                                   |                                              | Communicable diseases intelligence - Australian Government Department of Health | 2020 | 02/12 | 10.3331/cdh.2020.44.14 |
| Pre- and Posttreatment Chest CT Findings: 2019 Novel Coronavirus (2019-nCoV) Pneumonia | Duan YN, Qin J                               | Radiology - Radiological Society of North America | 2020 | 02/12 | doi.org/10.1148/radiol.2020200323 |
| First Case of 2019 Novel Coronavirus in the United States                    | Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, Spitters C, Ericson K, Wilkinson S, Tiral A, Diaz G, Cohn A, Fox L, Patel A, Greber SJ, Kim L, Tong S, Lu X, Lindstrom S, Pullansch MA, Weldon WC, Bigos HM, Uyeki TM, Pillai SR, Washington State 2019-nCoV Case Investigation Team | The New England Journal of Medicine               | 2020 | 01/31 | 10.1056/NEJMc2001199 |
| Use of Chest CT in Combination with Negative RT-PCR Assay for the 2019 Novel Coronavirus but High Clinical Suspicion | Huang P, Liu T, Huang L, Liu H, Li M, Xu W, Hu X, Chen J, Liu B | Radiology - Radiological Society of North America | 2020 | 02/12 | 10.1148/radiol.2020200330 |
| A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version) | Jin YH, Cai L, Cheng ZS, Cheng J, Deng T, Fan YF, Fang C, Huang D, Huang LQ, Huang Q, Han Y, Hu R, Hu F, Li BH, Li YR, Liang K, Liu LK, Luo LS, Ma J, Mu LL, Peng ZY, Pan YB, Pan ZY, Ren XQ, Sun HM, Wang Y, Wang YY, Weng H, Wei CF, Wu DF, Xia J, Xiong Y, Xu HB, Yao XM, Yuan YF, Ye TS, Zhang XC, Zhang YW, Zhang YG, Zhang HM, Zhao Y, Zhao MJ, Zi H, Zeng XT, Wang YY, Wang XR | Military Medical Research | 2020 | 02/06 | 10.1186/s00778-020-0333-4 |
| The First Case of 2019 Novel Coronavirus Pneumonia Imported into Korea from Wuhan, China: Implication for Infection Prevention and Control Measures | Kim JY, Cho PG, Oh Y, Oh KJ, Kim J, Park SJ | The Journal of Korean medical science             | 2020 | 02/10 | 10.3346/jkms.2020.35.e61 |
| Evolution of CT Manifestations in a Patient Recovered from 2019 Novel Coronavirus (2019-nCoV) Pneumonia in Wuhan, China | HeshuiShi, XiaoyuHan, ChuanshengZheng | Radiology - Radiological Society of North America | 2020 | 02/07 | 10.1148/radiol.2020200269 |
| Chest CT for Typical 2019-nCoV Pneumonia: Relationship to Negative RT-PCR Testing. | Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J | Radiology - Radiological Society of North America | 2020 | 02/12 | 10.1148/radiol.2020200343 |
| Changes of CT Findings in a 2019 Novel Coronavirus (2019-nCoV) pneumonia patient. | Fang X, Zhao M, Li S, Yang L, Wu B | Quarterly journal of medicine                     | 2020 | 02/19 | 10.1093/qjmed/hcaaf638 |
| Article title | List of authors | Journal name | Year | MM/DD | doi |
|----------------|----------------|--------------|-------|-------|-----|
| CT Manifestations of Two Cases of 2019 Novel Coronavirus (2019-nCoV) Pneumonia | Fang Y, Zhang H, Xu Y, Xie J, Pang P, Ju W | Radiology | 2020 | 02/07 | doi:10.1148/radiol.2020200280 |
| First cases of coronavirus disease 2019 (COVID-19) in France: surveillance, investigations and control measures, January 2020. | Bernard Storeckis S, Rolland P, Silue Y, Maillès A, Campese C, Simonoud A, Mescalin M, Maurice L, Nguyen M, Basi C, Yamani E, Behdill S, Ismail S, Nguyen D, Malvy D, Lexueux FX, Georges S, Lazarris C, Tobar A, Sempielet M, Enoul , Coupar B, Levy-Bruhl D | Eurosurveillance | 2020 | 02/13 | 10.2807/1560-7917.ES.2020.25.6.2000094 |
| Clinical Features and Treatment of 2019-nCoV Pneumonia Patients in Wuhan: Report of A Couple Cases | Zhang Z, Li X, Zhang W, Shi ZL, Zheng Z, Wang T | Viroligica Sinica | 2020 | 02/07 | doi.org/10.1007/s12251-020-00203-8 |
| The first 2019 novel coronavirus case in Nepal | Bastola A, Sah R, Rodriguez-Morales A, Lal BK, Jha R, Ojha HC, Shrestha B, Chu DKW, Poon LLM, Costello A, Mota K, Pandey BD | The Lancet Infectious Diseases | 2020 | 02/10 | 10.1016/S1473-3099(20)30067-0 |
| 2019-novel coronavirus infection in a three-month-old baby | Zhang YH, Lin DJ, Xiao MF, Wang JC, Wei Y, Lei ZX, Zeng ZQ, Li L, Li HA, Xiang W | Chinese journal of pediatrics | 2020 | 02/11 | 10.3760/cma.j.issn.0578-1310.2020.0006 |
| Clinical Characteristics and Therapeutic Procedure for Four Cases With 2019 Novel Coronavirus Pneumonia Receiving Combined Chinese and Western Medicine Treatment | Zhenwei Wang, Xiaorong Chen, Yanfei Chen, Wei Zhang | BioScience Trends | 2020 | 02/09 | 10.5582/bst.2020.01030 |
| RNA Based mNGS Approach Identifies a Novel Human Coronavirus From Two Individual Pneumonia Cases in 2019 Wuhan Outbreak | Liangjun Chen, Weiying Liu, Qi Zhang, Ke Xu, Guangming Ye, Wenchun Wu, Ziyou Sun, Fang Liu, Kailang Wu, Bo Zhong, Yi Mei, Wenxia Zhang, Ya Chen, Yirong Li, Miao Shi, Ke Lan, Yingle Liu | Emerging Microbes and Infections | 2020 | 01/29 | 10.1080/22221751.2020.1725399 |
| Novel Coronavirus Pneumonia Outbreak in 2019: Computed Tomographic Findings at Two Cases | Lin X, Gong Z, Xiao Z, Xiong J, Fan B, Liu J | Korean journal of radiology | 2020 | 02/11 | doi:10.3348/kjr.2020.0078 |