

1                    **Clinical and epidemiological characteristics of Coronavirus Disease 2019**  
2    **(COVID-19) patients**

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## 16 **Summary**

17

18 *Background:* Numerous groups have reported the clinical and epidemiological characteristics of  
19 Coronavirus Disease 2019 (COVID-19) cases; however, the data remained inconsistent. This  
20 paper aimed to pool the available data to provide a more complete picture of the characteristics  
21 of COVID-19 patients.

22

23 *Methods:* A systematic review and pooled analysis was performed. Eligible studies were  
24 identified from database and hand searches up to March 2, 2020. Data on clinical (including  
25 laboratory and radiological) and epidemiological (including demographic) characteristics of  
26 confirmed COVID-19 cases were extracted and combined by simple pooling.

27

28 *Results:* Of 644 studies identified, 69 studies (involving 48,926 patients) were included in the  
29 analysis. The average age of the patients was 49.16 years. A total of 51.46% of the patients  
30 were men and 52.32% were non-smokers. Hypertension (50.82%) and diabetes (20.89%) were  
31 the most frequent comorbidities observed. The most common symptoms were fever (83.21%),  
32 cough (61.74%), and myalgia or fatigue (30.22%). Altered levels of blood and biochemical  
33 parameters were observed in a proportion of the patients. Most of the patients (78.50%) had  
34 bilateral lung involvements, and 5.86% showed no CT findings indicative of viral pneumonia.  
35 Acute respiratory distress syndrome (28.36%), acute cardiac injury (7.89%) and acute kidney  
36 injury (7.60%) were the most common complications recorded.

37

38 *Conclusions:* Clinical and epidemiological characteristics of COVID-19 patients were mostly  
39 heterogeneous and non-specific. This is the most comprehensive report of the characteristics of  
40 COVID-19 patients to date. The information presented is important for improving our  
41 understanding of the spectrum and impact of this novel disease.

## 42 **Introduction**

43 There is an ongoing pandemic of viral pneumonia called Coronavirus Disease 2019 (COVID-19)  
44 which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.  
45 At the time of this writing, the disease has been reported to affect 634,835 people in more than  
46 200 countries, territories or areas, and cause 29,891 deaths (1). Understanding the clinical and  
47 epidemiological characteristics of the disease is important for informing public health decision  
48 making, which would enable improvement of surveillance and effective planning of treatment. In  
49 January 2020, Huang et al. (2) published the first report on the characteristics of a series of  
50 COVID-19 patients in Wuhan, China, the first epicenter of the outbreak. Following that, many  
51 other groups have reported the clinical and epidemiological features of COVID-19 patients, both  
52 in China and in other parts of the world (3-12). However, most of these reports were limited by a  
53 small sample size, and the characteristics reported appeared to be inconsistent. For example, in  
54 a report involving 99 patients, Chen et al. (3) noted a much higher proportion of men than  
55 women, and suggested that men were generally more susceptible to SARS-CoV-2 infection. On  
56 the other hand, Shi et al. (4) found that the male-to-female ratio among the 81 patients included  
57 was close to 1:1, indicating that both genders were equally susceptible to COVID-19. Recently,  
58 the World Health Organization (WHO) has declared COVID-19 a global pandemic and the  
59 contagion shows no sign of slowing down (13). Thus, it is a timely prompt to obtain a more  
60 precise understanding of the disease by combining all available data in the literature. In this  
61 study, a systematic review and pooled analysis was performed to characterize the clinical and  
62 epidemiological features of COVID-19 patients.

## 63 **Methods**

### 64 **Search strategy and selection criteria**

65 Three separate searches were performed on PubMed database on March 2, 2020, using the  
66 keywords “COVID-19”, “2019-nCoV” and “SARS-CoV-2”. No language restriction was applied.  
67 After removal of duplicated records, screening by title and abstract was performed to identify  
68 potentially relevant studies. The full-texts of these potentially relevant studies were then  
69 evaluated. The reference lists of these studies were also hand-searched to identify additional  
70 records. Studies were included if they reported any clinical and/or epidemiological data of  
71 confirmed COVID-19 patients, regardless of their study design. However, review papers or  
72 studies employing secondary analysis of the previously available data were excluded from the  
73 analysis. In case of overlapping studies, the ones which the largest sample size or the most  
74 complete data set were included.

75

### 76 **Data analysis**

77 The following data were extracted from the included studies: name of first author, country, date  
78 of diagnosis, demographic data, smoking status, comorbidities, signs and symptoms,  
79 laboratory/biochemical data, CT findings, and complications of the disease. A simple pooling of  
80 data was performed to provide an overall summary of the clinical and epidemiological  
81 characteristics of the patients. All data are reported as absolute number and/or mean. As  
82 patient-level data were not available in majority of the studies, standard deviation could not be  
83 calculated.

84

### 85 **Role of the funding source**

86 There was no funding source for this study. The corresponding author had full access to all the  
87 data in the study and had final responsibility for the decision to submit for publication.

## 88 Results

89 The flowchart of study selection is depicted in Figure 1. A total of 644 records were identified  
90 from the PubMed searches. After deduplication, 517 unique records were identified. Following  
91 screening by title and abstract, 440 records were removed and full-texts of the remaining 77  
92 studies were retrieved for assessment of eligibility. Five records were subsequently removed as  
93 they reported secondary data or contained insufficient data on clinical and/or epidemiological  
94 characteristics of the patients. In addition, three overlapping records were excluded. Eventually,  
95 69 studies were included in the current analysis (2-12, 14-71). These 69 studies comprised a  
96 total of 48,926 confirmed COVID-19 patients, although only appropriate subcohorts were used  
97 in the analysis of each clinical/epidemiological characteristic. A great majority of these studies  
98 were from mainland China, while five were from Korea and one each from the USA, Germany,  
99 France, Australia, Italy, Singapore, Vietnam, Nepal, Hong Kong, and Taiwan.

100

101 The characteristics of the patients are shown in Table 1. The mean age of the patients  
102 was 49.16 years. The number of male patients was slightly higher than that of female (51.46%  
103 vs. 48.54%), and the number of non-smokers was slightly higher than that of smokers (52.32%  
104 vs. 47.68%). A minority (25.93%) of the patients had comorbidities, among which hypertension  
105 was the most common (50.82%), followed by diabetes (20.89%), cardiovascular and  
106 cerebrovascular diseases (16.54%), respiratory system disease (9.70%) and malignancy  
107 (2.05%). Most of the patients showed at least one sign or symptom at presentation, with only  
108 0.8% of the patients were asymptomatic. The most common symptoms seen included fever  
109 (83.21%), cough (61.74%), myalgia or fatigue (30.22%), sputum production (20.22%), and  
110 dyspnea (16.97%). On average, the length from illness onset to dyspnea was 4.99 days.

111

112 The laboratory findings of the patients are also shown in Table 1. Majority (63.06%) of  
113 the patients had a normal leukocyte count, but as much as 24.14% and 12.80% respectively

114 showed decreased and increased leukocyte counts. Besides, 51.39% of the patients had a  
115 decreased lymphocyte count and 9.63% had a decreased platelet count. Increased levels of  
116 aspartate aminotransferase, creatinine, creatine kinase, lactate dehydrogenase, hypersensitive  
117 troponin I, procalcitonin and C-reactive protein were observed in 27.45%, 5.19%, 13.25%,  
118 45.76%, 3.57%, 69.08% and 72.30% of the patients, respectively.

119

120 Analysis of computed tomography (CT) data revealed that most of the patients (78.50%)  
121 had bilateral lung involvements, while 15.65% had unilateral lung involvements and 5.86%  
122 showed no sign of viral pneumonia. In 41.18% of the patients, all five lung lobes were affected.  
123 On the other hand, as much as 17.03%, 11.46%, 12.69% and 17.65% patients respectively had  
124 one, two, three and four lobes affected.

125

126 It was unknown how many patients had complications following SARS-CoV-2 infection.  
127 Nonetheless, among the wide spectrum of complications observed, acute respiratory distress  
128 syndrome (ARDS) was most frequently documented (28.36%), followed by acute cardiac injury  
129 (7.89%) and acute kidney injury (7.60%).

130 **Discussion**

131 COVID-19 poses a significant burden on the healthcare system all over the world. A complete  
132 understanding of the characteristics of the disease is important for effective surveillance and  
133 public health response measures to be implemented in a timely manner. Currently, although we  
134 have some basic understanding of the clinical and epidemiological features of COVID-19  
135 patients, our knowledge is insufficient. This is because inconsistencies still exist in the findings  
136 of many published reports, and the sample sizes in most of these reports were too small for a  
137 reliable summary to be made. In this work, a systematic review and pooled analysis was  
138 performed to combine data from 69 previous reports, in order to yield a more accurate summary  
139 of the clinical and epidemiological characteristics of COVID-19 patients.

140

141 In many instances, susceptibility to viral infections may be related to factors such as  
142 gender and smoking habits (72-74). For the former, it is believed that X chromosome  
143 inactivation in females may cause cellular mosaicism which ensures the presence of at least  
144 one functional copy of X-linked immune genes, thus conferring women an increased resistance  
145 against viral infections (75). In addition, estrogen, the major female sex hormone, is known to  
146 promote adaptive immune response (76), while testosterone, the primary sex hormone in men,  
147 could contribute to the suppression of the innate immune response, rendering men more  
148 susceptible to viral infections (77, 78). On the other hand, cigarette smoking may reduce the  
149 level of circulating immunoglobulins, immune cells, and pro-inflammatory cytokines, as well as  
150 disrupt the response of antibodies to antigens (72). For these reasons, some studies have  
151 suggested that men and smokers are more susceptible to SARS-CoV-2 infections (3, 79). In the  
152 present work, we noted that the ratios of male to female and smokers to non-smokers were  
153 close to 1:1. Although the relative risk or odds ratio of the association between these variables  
154 and SARS-CoV-2 infection could not be computed due to the lack of a comparison group, a  
155 proportion of approximately 1:1 suggests that susceptibility to SARS-CoV-2 infection is universal.

156

157           The present work also showed that the symptoms of COVID-19 were generally non-  
158 specific, thus the disease cannot be reliably distinguished from other infectious diseases based  
159 on the symptoms alone. The most commonly observed symptoms were similar to those of the  
160 previous coronavirus disease outbreaks (MERS and SARS), i.e. fever, cough, and myalgia or  
161 fatigue. Nevertheless, compared to MERS and SARS, the proportion of afebrile patients was  
162 much higher in COVID-19 (16.79% cf. 2% in MERS and 0-1% in SARS) (80). This indicates that  
163 a significant number of COVID-19 patients would be missed if surveillance and monitoring  
164 systems focus largely on temperature screening, as commonly practiced in airports (81, 82).  
165 The present work also showed that dyspnea was observed in only 16.97% of the patients. This  
166 contradicts with advisories and guidelines published by many health authorities, which suggest  
167 that dyspnea is a commonly observed symptom in COVID-19 (83-89). Besides, it was observed  
168 that 0.80% of the patients were asymptomatic. Currently, whether asymptomatic patients can  
169 transmit the virus to other individuals is not fully known, but it is highly possible (35). Thus,  
170 although the number of asymptomatic patients was low, identifying and isolating such patients  
171 to prevent uncontrolled disease spread would prove very challenging. It is therefore important  
172 for diagnostic tests to be performed on asymptomatic medium- and high-risk individuals to  
173 facilitate early detection and prevention of SARS-CoV-2 transmission. In addition to nucleic acid  
174 testing using real-time reverse transcription polymerase chain reaction, some studies have  
175 suggested the potential usability of chest CT for COVID-19 diagnosis (90, 91). However, in the  
176 present work, we found that 5.86% of the patients did not have abnormalities on CT scans. Thus,  
177 although CT findings have substantial accuracy in identifying the disease (90, 91), the results need  
178 to be interpreted with caution.

179

180           SARS-CoV-2 is known to infect a cell by first binding to its angiotensin converting  
181 enzyme 2 (ACE2) receptor (92). Apart from the lung, high expression of ACE2 receptor is also

182 observed in several other organs such as the heart, kidney, and intestine, as well as the in  
183 lymphocytes (93, 94). Several previous studies reported that a decreased lymphocyte count  
184 was a common feature of SARS-CoV-2 infection (2, 3, 7, 30, 41). In the present work,  
185 lymphopenia was observed in 51.39% of the patients. A decreased lymphocyte count implies a  
186 weakening adaptive immune system. Considering the high expression of ACE2 in lymphocytes,  
187 it has been postulated that SARS-CoV-2 may directly infect and attack lymphocytes, thus  
188 impairing the immune system (95). Besides the decrease in lymphocyte count, the present  
189 study also showed that many COVID-19 patients had increased levels of C-reactive protein,  
190 creatine kinase, lactate dehydrogenase and procalcitonin. High levels of C-reactive protein and  
191 creatine kinase suggest that sustained inflammatory response occurs following SARS-CoV-2  
192 infection, whereas high levels of lactate dehydrogenase and procalcitonin indicate the virus  
193 could, either directly or indirectly, cause tissue injury. A previous work reported that a low  
194 lymphocyte count and high levels of lactate dehydrogenase and C-reactive protein were among  
195 the parameters found to be correlated with severity of lung injury in COVID-19 patients, as  
196 measured using the Murray scores (17). Nonetheless, the relationship between these variables  
197 and severity of COVID-19 was not investigated in the present work due to the insufficient data  
198 available.

199

200 A few limitations exist in the present work. First, there were instances where a same  
201 patient was described in multiple reports (15, 96). Efforts have been made to identify such  
202 patients by meticulously reviewing the descriptions of the patients in each report. However,  
203 since all patients were anonymized, it was challenging to identify all overlapping patients. Thus,  
204 there is a possibility that some overlapping patients were not removed from our analysis and  
205 their characteristics were overreported. Besides, since patient-level data were not reported in  
206 most of the studies, median values and standard deviations, which understandably provide  
207 more meaningful information, could not be computed. Finally, as mentioned above, various

208 comparisons among the patients (e.g. severe vs. mild, and death vs. survivor) could not be  
209 analyzed due to insufficient data available.

210

## 211 **Conclusion**

212 In conclusion, this report has successfully provided a more complete picture of the clinical and  
213 epidemiological characteristics of COVID-19 patients. A wide variation exists in the clinical  
214 manifestation of the disease. As the outbreak continues to escalate and SARS-CoV-2 continues  
215 to mutate (97), it is important to consistently update the characteristics of the patients in order to  
216 monitor whether evolving strains of the virus could cause the disease differently. Sharing of  
217 clinical and epidemiological data among the scientific community is highly important for  
218 informing public health decision making for controlling the spread of the disease.

219 **Contributor**

220 SCT contributed solely to this work.

221

222 **Declaration of interests**

223 The author declares no competing interests.

224

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492 Table 1: Characteristics of COVID-19 patients

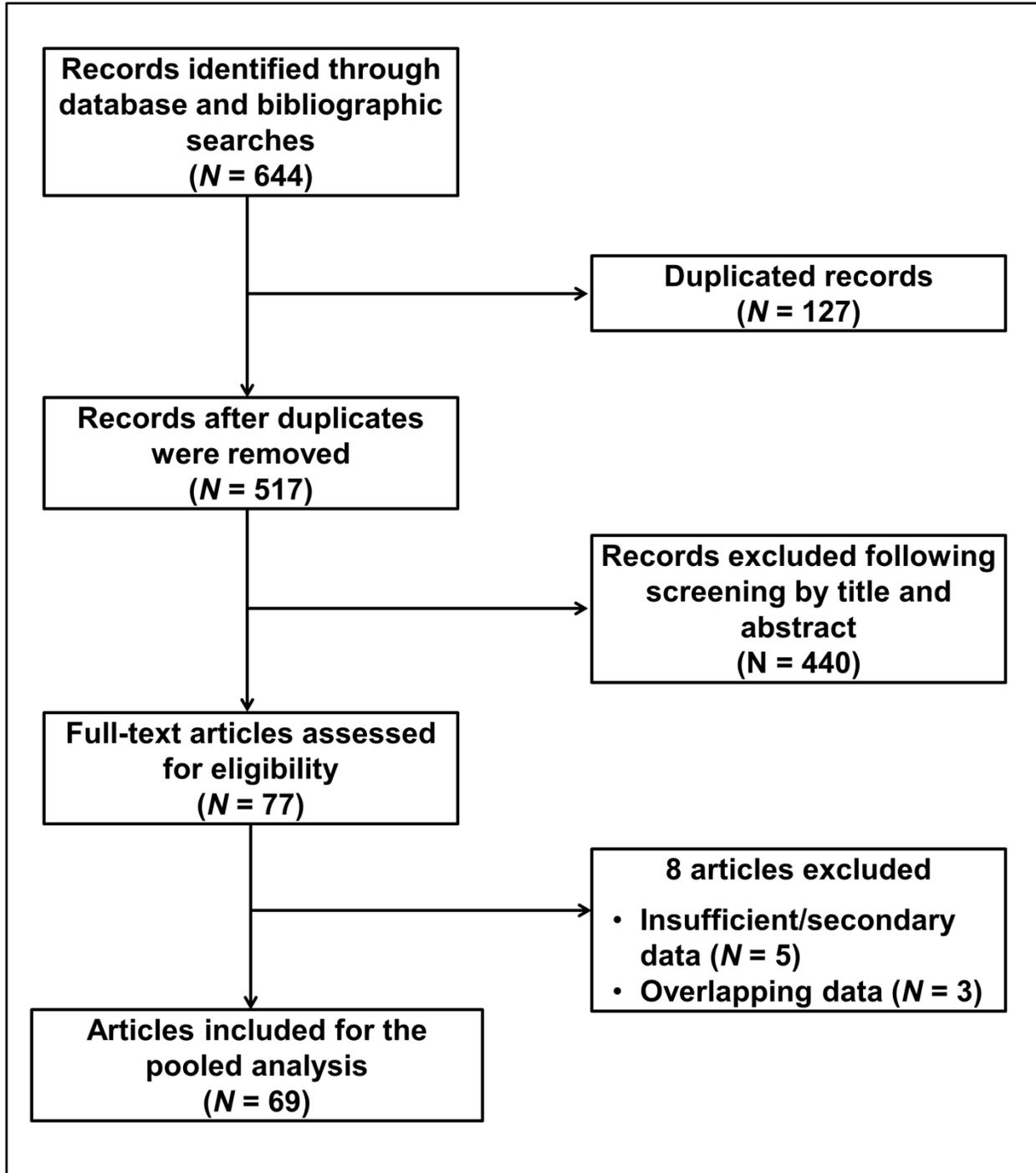
Characteristics	Number of patients analyzed	Number/Mean
Age (years)	1,725	49.16
Sex	44,760	
Male		23,032 (51.46%)
Female		21,728 (48.54%)
Smoking status	2,030	
Smokers		968 (47.68%)
Non-smokers		1,062 (52.32%)
Comorbidities	21,020	
Yes		5,451 (25.93%)
No		15,569 (74.07%)
Type of comorbidities	5,450	
Hypertension		2,683 (50.82%)
Diabetes		1,103 (20.89%)
Cardiovascular and cerebrovascular diseases		873 (16.54%)
Respiratory system disease		512 (9.70%)
Malignancy		108 (2.05%)
Presence of symptoms	3,117	
Yes		3092 (99.20%)
No		25 (0.80%)
Signs and symptoms		
Fever	3,097	2577 (83.21%)
Cough	3,097	1912 (61.74%)
Myalgia or fatigue	3,117	942 (30.22%)
Sputum production	3,115	630 (20.22%)
Dyspnea	3,093	525 (16.97%)
Length from illness onset to dyspnea (days)	179	4.99
Headache	3,114	325 (10.44%)
Sore throat	3,117	250 (8.02%)
Chill	3,117	201 (6.45%)
Nausea and vomiting	3,116	142 (4.56%)
Diarrhea	3,113	136 (4.37%)
Chest tightness but not pain	3,117	94 (3.02%)
Nasal congestion or runny nose	3,117	64 (2.05%)
Loss of appetite	3,116	62 (1.99%)
Abdominal pain	3,116	38 (1.22%)
Rhinorrhoea	3,117	35 (1.12%)
Pharyngalgia	3,117	33 (1.06%)
Dizziness	3,117	32 (1.03%)
Chest pain	3,117	25 (0.80%)
Hemoptysis	3,115	23 (0.74%)
Respiratory rate >24 breaths per min	3,117	22 (0.71%)
Malaise	3,117	21 (0.67%)
Heart palpitation	3,117	14 (0.45%)
Conjunctivitis	3,117	10 (0.32%)
Confusion	3,117	10 (0.32%)
Blood in sputum	3,117	3 (0.10%)
Anthralgia	3,117	2 (0.06%)

Gastrointestinal reaction	3,117	1 (0.03%)
Back pain	3,117	1 (0.03%)
Constipation	3,117	1 (0.03%)
Skin tingling	3,117	1 (0.03%)
Somnolence	3,117	1 (0.03%)
Sneezing	3,117	1 (0.03%)
Jaundice	3,117	1 (0.03%)
Respiratory symptoms*	3,117	7 (0.22%)
Laboratory findings		
Leukocyte count ( $\times 10^9$ per L)	801	5.60
Decreased	961	232 (24.14%)
Normal	961	606 (63.06%)
Increased	961	123 (12.80%)
Neutrophil count ( $\times 10^9$ per L)	571	3.63
Lymphocyte count ( $\times 10^9$ per L)	849	0.97
Decreased	827	425 (51.39%)
Normal	827	402 (48.61%)
Hemoglobin, g/L	336	127.47
Platelet count, ( $10^9$ per L)	635	181.58
Decreased	561	54 (9.63%)
Prothrombin time (s)	562	11.94
Activated partial thromboplastin time (s)	360	29.96
D-dimer (mg/L)	726	1.13
D-dimer (mg/L) when one study was removed <sup>†</sup>	645	0.45
Albumin (g/L)	473	36.84
Alanine aminotransferase (U/L)	634	31.55
Aspartate aminotransferase (U/L)	614	32.59
Normal	499	362 (72.55%)
Increased	499	137 (27.45%)
Total bilirubin (mmol/L)	659	12.04
Potassium (mmol/L)	44	4.23
Sodium (mmol/L)	44	138.48
Creatinine ( $\mu\text{mol/L}$ )	633	72.45
Normal	231	219 (94.81%)
Increased	231	12 (5.19%)
Creatine kinase (U/L)	636	93.66
Normal	400	347 (86.75%)
Increased	400	53 (13.25%)
Lactate dehydrogenase (U/L)	547	261.44
Normal	413	224 (54.24%)
Increased	413	189 (45.76%)
Hypersensitive troponin I (pg/mL)	179	5.91
>28 (99th percentile)	28	1 (3.57%)
Procalcitonin (ng/mL)	334	0.21
Normal	359	111 (30.92%)
Increased	359	248 (69.08%)
Increased C-reactive protein	870	629 (72.30%)
CT findings		
Lung involvement	1,144	
Bilateral		898 (78.50%)
Unilateral		179 (15.65%)

No abnormalities		67 (5.86%)
Number of lobes affected	323	
1		55 (17.03%)
2		37 (11.46%)
3		41 (12.69%)
4		57 (17.65%)
5		133 (41.18%)
Complications	342	
Acute respiratory distress syndrome		97 (28.36%)
Acute cardiac injury		27 (7.89%)
Acute kidney injury		26 (7.60%)
Arrhythmia		23 (6.73%)
Shock		20 (5.85%)
Hyperglycemia		18 (5.26%)
Hepatic insufficiency / liver dysfunction		17 (4.97%)
Acute respiratory injury		8 (2.34%)
Hospital acquired/Ventilator associated pneumonia		8 (2.34%)
RNAemia		6 (1.75%)
Secondary infection		4 (1.17%)
Renal insufficiency		2 (0.58%)
Gastrointestinal hemorrhage		2 (0.58%)
Cardiac failure		1 (0.29%)
Pneumothorax		1 (0.29%)
Urinary tract infection		1 (0.29%)
Bacteremia		1 (0.29%)

\* Respiratory symptoms included multiple symptoms such as cough and sore throat, but they were not reported separately in the original publications

† Data from Shi et al. (4) was removed as the value reported was an outlier



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495 Figure 1: Flow chart of study selection