Clinical features and laboratory findings of SARS-CoV-2 infection in hospitalized patients

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Abstract

Background: Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), is a new emerging public health crisis to the world. However, data are still limited on the clinical features and laboratory findings in COVID-19 patients.

Methods: Medical records including demographics characteristics, clinical features, laboratory findings and radiological materials of 66 hospitalized COVID-19 patients were collected between Jan 23 and Mar 9, 2020. Symptoms/signs with potential association with the disease severity were analyzed.

Results: Of 66 hospitalized COVID-19 patients, the male-to-female ratio was 44:22. There were eight cases potentially exposed to one single patient. The most common initial symptoms of SARS-CoV-2 infection were fever (77.3%) and cough (74.2%). Compared to those with non-severe infection, the severe patients were more likely to be older (62.6 ± 15.1 *vs* 46.9 ± 13.3 years. $P = 0.001$) and with more infected lobes. As the results shown, higher initial (on admission) and peak (during hospitalization) counts of lymphocyte were inversely associated with the severe SARS-CoV-2 infection (both OR: 0.01 every $1´10^9$/L decrease). However, the elevated initial neutrophil counts (OR: 1.63 every $1´10^9$/L increase), initial and peak levels of LDH (OR: 1.02 and 1.01 every 1 U/L increase), peak levels of CRP (OR: 1.03 every 1 mg/L increase), AST (OR: 1.06 every 1 U/L increase) and ALT (OR: 1.02 every 1 U/L increase) were significantly associated with COVID-19 severity.

Conclusion: Our present study indicated that fever and cough were the most common initial symptoms of SARS-CoV-2 infection, and the virus could be efficiently spread by person-to-person transmission. In addition, lymphocyte and neutrophil counts, and serum levels of AST, ALT, CRP and LDH should be useful for the evaluation on COVID-19 severity.

Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of Coronavirus disease 2019 (COVID-19), is a new emerging public health crisis threatening the world [1,2]. As of 03/30/2020, SARS-CoV-2 has rapidly spread to about 200 countries. In addition, more than 700,000 COVID-19 cases and around 20,000 deaths have been reported worldwide [3]. Recently, several modelling studies suggested that the basic case reproduction number of SARS-CoV-2 was estimated to range from 2 to 6.47, indicating that the virus possesses powerful transmissibility, being more infectious than SARS-CoV and MERS-CoV [4,5].

Clinical features, epidemiological history and laboratory findings are important in the diagnosis of COVID-19, where making an accurate decision in time is necessary to control the virus transmission. Until now, dozens of reports have described the clinical characteristics of SARS-CoV-2 infection, including the temporal progression of clinical symptoms, chest radiography, outcomes, and risk factors for the severity of the disease [6-8]. However, data are still limited on the laboratory findings in COVID-19 patients, such as leukopenia, lymphopenia, thrombocytopenia, creatine kinase (CK), lactate dehydrogenase (LDH),

aspartate aminotransferase (AST), alanine aminotransferase (ALT), C-reactive protein (CRP) and the associations of these routine laboratory indexes with severe SARS-CoV-2 infection, which is estimated to be 15-20% of totally confirmed cases according to the previous studies [9-10].

The objective of this retrospective study was to analyze the clinical and laboratory characteristics of 66 hospitalized COVID-19 cases, with emphasis on the possible person-to-person transmission, laboratory findings and risk factors for the disease severity of SARS-CoV-2 infection.

Methods

Setting and patients

Huai'an Fourth People's Hospital is an 800-bed, university-affiliated medical center. It is the sole hospital caring for COVID-19 patients in Huai'an city, which is located in the hinterland of Northern Jiangsu, China, with a population of 5.68 million people.

The present analysis was performed of 66 hospitalized patients with SARS-CoV-2 infection, who were admitted to Huai'an Fourth People's Hospital between Jan 23 and Mar 9, 2020. Diagnosis of COVID-19 was based on the "New Coronavirus Pneumonia Prevention and Control Program (3-5th version)" published by the National Health Commission of China [11-13]. In the present study, patients co-infected with two or more pathogens were excluded. This retrospective study was reviewed and approved by the Medical Ethical Committee of Huai'an Forth people's Hospital (approval number HASY2020004) in accordance with the Declaration of Helsinki for Human Research of 1974. A waiver of informed consent was obtained.

Laboratory test

Pharyngeal swab specimens and blood samples were collected from each patient on admission day. All samples were processed simultaneously at the Department of clinical laboratory of Huai'an Fourth People's Hospital. The SARS-CoV-2 RNA was isolated from pharyngeal swab specimen and tested using qRT-PCR kits (BGI Genomics, Beijing, China), which was recommended by the Chinese Center for Disease Control and Prevention (CDC). The other routine laboratory tests, including lymphocyte counts, neutrophil counts, and serum levels of AST, ALT, CK, LDH and CRP were measured using commercial reagents according to the manufacture's introductions. All of laboratory tests were examined within 24 hours of hospital admission.

Diagnostic criteria and data collection

Severity of COVID-19 was determined with the "New Coronavirus Infected Pneumonia Diagnosis and Treatment Program (3-5th version)" [11-13] as following: (1) Mild cases: the clinical symptoms were mild, and there was no sign of pneumonia on imaging; (2) Moderate cases: only showing fever and respiratory symptoms with radiological findings of pneumonia; (3) Severe cases (for adults): ▯ Respiratory distress ≥

30 breaths/ min; ▯ Oxygen saturation ≤ 93% at rest; ▯ Arterial partial pressure of oxygen (PaO2)/fraction of inspired oxygen (FiO2)≤ 300mmHg; (4) Critical cases: ▯ Respiratory failure and requiring mechanical ventilation; ▯ Shock; ▯ With other organ failure that requires intensive care unit (ICU) care.

Detailed contact history of each case was recorded upon admission, including the travel history in Hubei, the date/time of suspected contact, and the symptoms onset after contacting with the confirmed cases. The symptoms presented on each case upon admission were also recorded, including fever, cough, fatigue, myalgia, asthma, etc. All included patients were examined by computed tomography (CT) within 24 hours of hospital admission. In addition, the underlying diseases in each patient were collected on admission.

Statistical analysis

All statistical analysis was performed with SPSS version 21.0 (SPSS Inc., https://www.ibm.com/analytics/spss-statistics-software). In the present study, COVID-19 patients were classified into non-severe (mild/moderate) and severe (severe/critcal) groups. Means (standard deviations) or medians (interquartile) were calculated as summaries of continuous variables. For categorical variables, percentages of patients in each category were calculated. An independent samples *t*-test, chi-square test, Fisher's exact test or non-parametric test was used to compare the clinical characteristics and laboratory findings between the patients with and without severe COVID-19, as appropriate. The odds ratios (OR) and the corresponding 95% confidence intervals (CI) were calculated using multivariate logistic regression analysis, adjusted for age and gender. A two-sided P value < 0.05 was defined as statistically significant.

Results

The demographic and clinical characteristics of 66 patients were presented in Table 1. The male-to-female ratio was 44:22, and the two most common initial symptoms of SARS-CoV-2 infection were fever (77.3%) and cough (74.2%). As the results shown, five, 50 and 11 patients were diagnosed as mild, moderate and severe cases, respectively. No critical case was determined according to the criteria. Compared to the non-severe cases (mild/moderate), the severe patients were more likely to be older (62.6 ± 15.1 *vs* 46.9 ± 13.3 years. P = 0.001). However, no significant difference in the length of hospital stay between the severe and non-severe patients (18.6 ± 8.0 *vs* 15.9 ± 4.0 days, P = 0.094). In addition, 38.2% of non-severe patients and 63.6% of severe patients coexisted with various underlying diseases, respectively (= 2.432, P = 0.182).

Table 1 Demographic characteristics and initial clinical signs/symptoms of 66 COVID-19 patients

Symptoms/signs	Mean±SD/cases (%)
Sex	
Male (no., %)	44 (66.7)
Female (no., %)	22 (33.3)
Age (years)	
Non-severe cases	46.9 ± 13.3
Severe cases	62.6 ± 15.1
Clinical classification (no., %)	
Mild	5 (7.6)
Ordinary	50 (75.7)
Severe	11 (16.7)
Initial symptoms (no., %)	
Fever	51 (77.3)
Cough	49 (74.2)
Fatigue	20 (30.3)
Myalgia	16 (24.2)
Asthma	15 (22.7)
Chest tightness	14 (21.2)
Sore throat	11 (16.7)
Diarrhea	3 (4.5)
Vomiting	2 (3.0)
Headache	1 (1.5)
Dyspnea	1 (1.5)
Underlying disease (no., %)	
Non-severe	21 (38.2)
Severe	7 (63.6)
Length of hospital stay (days)	
Non-severe	15.9 ± 4.0
Severe	18.6 ± 8.0

Non-severe patients including mild and moderate cases

The medical records and epidemiological history of each case revealed that there were eight cases potentially exposed to one single patient (Case 2) (Fig. 1). Case 2, a 48-year-old man, was the only patient of this cluster that had been in Wuhan, China. When he returned from Wuhan on Jan 15, 2020, he had a cough but without treatment. On Jan 25, 2020, his father (Case 5) and mother (Case 6) developed fever (the highest temperature was 38.8°C), cough and asthma. On Jan 18, 2020, Case 2 went to have a bath in a public bathhouse. Case 28, who took a bath together with Case 2, developed fever on Jan 25, 2020 and was demonstrated positive for the SARS-CoV-2 on Feb 3, 2020. Subsequently, the persons who closely contacted with Case 28, including his father (Case 27), father-in-law (Case 18), wife (Case 25) and two colleagues (Case 24 and 31) were diagnosed as COVID-19 between Feb 1 and Feb 3, 2020. Among nine patients, Case 2 and 6 showed severe symptoms and needed ticosteroids treatment, mechanical ventilation, or admission to ICU. The remaining seven patients were determined as mild or moderate SARS-CoV-2 infection. As of Feb 28, 2020, all cases have fully recovered and been discharged from the hospital.

Abnormalities on chest radiography suggesting pneumonia were occurred in all included patients. As the results shown, lesions were found in one lobe in two patients (mild: 1; moderate: 1), two lobes in eight patients (mild: 3; moderate: 5), three lobes in four patients (mild: 1; moderate: 3) and four lobes in 52

patients (moderate: 41; severe: 11). The duration from disease onset to the time when abnormalities on the chest radiography were first noted was 1-18 days (median 7 days).

The laboratory data on admission were listed in Table 2. The patients with severe COVID-19 were more likely to be with higher neutrophil counts, lower lymphocyte counts, and elevated levels of AST, LDH and CRP. During the hospitalization (Table 3), the peak levels of AST, LDH and CRP in severe COVID-19 patients were much higher than those in mild and moderate cases. However, lower lymphocyte counts increased the severity rate for SARS-CoV-2 infection.

Table 2 Laboratory characteristic of mild, moderate and severe hospitalized patients with SARS-CoV-2 infection on admission

Laboratory indexes	Clinical symptoms			*P*
	Mild	Moderate	Severe	
Leukocyte counts (´10^9/L)	4.6 ± 1.7	4.8 ± 1.6	6.5 ± 4.3	0.342
Lymphocyte counts (´10^9/L)	1.6 ± 0.9	1.3 ± 0.5	0.5 ± 0.2	<0.001
Neutrophil counts (´10^9/L)	2.6 ± 0.9	3.1 ± 1.3	5.7 ± 4.2	0.013
Platelet counts (´10^9/L)	172.0 ± 42.7	153.6 ± 42.6	149.5 ± 57.7	0.640
CRP levels (mg/L)	6.4 ± 6.9	31.2 ± 34.2	75.3 ± 73.2	0.006
ALT levels (U/L)	28.0 ± 8.5	31.7 ± 18.7	41.5 ± 28.7	0.322
AST levels (U/L)	24.4 ± 8.8	26.4 ± 12.1	38.6 ± 17.4	0.018
LDH levels (U/L)	183.6 ± 40.4	221.7 ± 65.8	306.9 ± 104.4	0.013
CK levels (U/L)	120.4 ± 82.0	84.4 ± 70.9	97.7 ± 72.3	0.520

CRP: C-reactive protein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; CK: creatine kinase

Table 3 Laboratory characteristics of mild, moderate and severe patients with SARS-CoV-2 infection during hospitalization

Laboratory indexes	Clinical symptoms			*P*
	Mild	Moderate	Severe	
Lowest leukocyte counts (´10^9/L)	4.3 ± 1.3	4.0 ± 1.0	3.4 ± 1.2	0.170
Lowest lymphocyte count (´10^9/L)	1.2 ± 0.5	1.0 ± 0.4	0.4 ± 0.2	<0.001
Lowest neutrophil count (´10^9/L)	2.5 ± 0.8	2.3 ± 0.7	2.3 ± 0.7	0.757
Lowest platelet counts (´10^9/L)	163.8 ± 49.6	142.0 ± 40.3	116.6 ± 59.1	0.110
Peak CRP level (mg/L)	19.1 ± 20.8	44.8 ± 43.0	162.5 ± 72.4	<0.001
Peak ALT level (U/L)	39.0 ± 21.2	54.3 ± 37.2	80.7 ± 49.8	0.074
Peak AST level (U/L)	26.4 ± 10.3	33.5 ± 15.9	66.1 ± 38.6	0.005
Peak LDH level (U/L)	189.6 ± 40.8	262.1 ± 101.2	426.1 ± 234.0	0.002
Peak CK level (U/L)	139.4 ± 76.2	116.7 ± 110.0	204.6 ± 206.5	0.129

CRP: C-reactive protein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; CK: creatine kinase

As the results shown in Table 4, multivariate logistic analysis suggested that higher initial (on admission) and peak (during hospitalization) counts of lymphocyte were inversely associated with the severe SARS-CoV-2 infection (both OR: 0.01 every 1´10^9/L decrease). However, the elevated initial neutrophil counts (OR: 1.63 every 1´10^9/L increase), initial and peak levels of LDH (OR: 1.02 and 1.01 every 1 U/L increase), peak levels of CRP (OR: 1.03 every 1 mg/L increase), AST (OR: 1.06 every 1 U/L increase) and ALT (OR: 1.02 every 1 U/L increase) were significantly associated with COVID-19 severity.

Table 4 Multivariate logistic regression analysis of laboratory indexes for severe COVID-19 in hospitalized patients

Laboratory indexes	OR(95% CI)[a]	P^a	OR(95%CI)[b]	P^b
Initial leukocyte counts (every 1× 10^9/L)	1.32 (0.98-1.77)	0.064	1.29 (0.97-1.72)	0.085
Initial lymphocyte count (every 1× 10^9/L)	0.01 (0.001-0.02)	0.001	0.01 (0.001-0.05)	0.002
Initial neutrophil count (every 1× 10^9/L)	1.82 (1.17-2.84)	0.009	1.63 (1.04-2.55)	0.033
Initial platelet count (every 1 × 10^9/L)	1.00 (0.98-1.01)	0.694	1.00 (0.98-1.01)	0.812
Initial CRP level (every 1 mg/L)	1.02 (1.00-1.04)	0.013	1.02 (0.99-1.04)	0.077
Initial ALT level (every 1 U/L)	1.02 (0.99-1.05)	0.157	1.03 (0.99-1.06)	0.147
Initial AST level (every 1 U/L)	1.06 (1.01-1.11)	0.015	1.05 (0.99-1.11)	0.104
Initial LDH level (every 1 U/L)	1.01 (1.00-1.02)	0.003	1.02 (1.00-1.03)	0.006
Initial CK level (every 1 U/L)	1.00 (0.99-1.01)	0.669	1.00 (0.99-1.01)	0.960
Lowest leukocyte counts (every 1 × 10^9/L)	0.54 (0.27-1.08)	0.082	0.56 (0.27-1.19)	0.134
Lowest lymphocyte count (every 1 × 10^9/L)	0.01 (0.001-0.01)	0.001	0.01 (0.001-0.03)	0.002
Lowest neutrophil count (every 1 × 10^9/L)	0.83 (0.32-2.16)	0.695	0.91 (0.31-2.63)	0.856
Lowest platelet count (every 1 × 10^9/L)	0.99 (0.97-1.00)	0.073	0.99 (0.97-1.01)	0.208
Peak CRP level (every 1 mg/L)	1.03 (1.02-1.05)	<0.001	1.03 (1.01-1.06)	0.002
Peak ALT level (every 1 U/L)	1.02 (1.00-1.03)	0.047	1.02 (1.00-1.04)	0.016
Peak AST level (every 1 U/L)	1.06 (1.02-1.10)	0.003	1.06 (1.02-1.11)	0.005
Peak LDH level (every 1 U/L)	1.01 (1.00-1.01)	0.006	1.01 (1.00-1.01)	0.023
Peak CK level (every 1 U/L)	1.00 (0.99-1.01)	0.069	1.00 (0.99-1.01)	0.160

CRP: C-reactive protein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; CK: creatine kinase

[a]Unadjusted model.

[b]Adjusted for age and gender.

Discussion

Clinical knowledge of potential factors related to the disease progression is critical for the management of COVID-19 patients. Similar to the previous findings [14,15], we observed that fever and cough were the two most common initial symptoms of SARS-CoV-2 infection, and 16.7% of hospitalized COVID-19 patients were determined as severe cases. In addition, severe COVID-19 patients were obviously older, and with more infected lobes compared to those with non-severe infection. Furthermore, we reported here that there were eight COVID-19 cases potentially exposed to one single patient, supporting that SARS-CoV-2 could be efficiently spread by person-to-person transmission.

In addition, our present results showed that both initial LDH level on admission and peak LDH level during hospitalization were positively associated with the severe SARS-CoV-2 infection. LDH is a non-specific enzyme found ubiquitously in cells [16]. Although the knowledge of the association between LDH and COVID-19 severity is limited, previous studies demonstrated strong evidence of an elevated risk for developing adverse outcomes or acute respiratory distress syndrome in SARS patients with elevated LDH [17,18]. In addition, Chang *et al*. reported that increased serum LDH level was significantly associated with several pulmonary infections, including tuberculosis and bacterial pneumonia [19]. Thus, serum LDH level might be helpful for the evaluation on the COVID-19 patients with severe pneumonia.

CRP is one of the most sensitive acute-phase reactants and is virtually absent from blood serum in the healthy person [20]. Previously, Singh *et al*'s study in Singapore suggested that 7 of 11 SARS patients had elevated CRP with a higher proportion in fatalities than in survivors (75% vs. 25%) [21]. In addition, Wang *et al*. found that 77.9% of SARS patients with elevated CRP on admission were at higher risk of fatality (OR = 1.447 for every 1 mg/L increase, $P = 0.006$) [22]. Recently, Zhang *et al*. reported that most severe SARS-CoV-2 infection patients exhibited higher levels of CRP compared to non-severe patients [23]. Similar to these findings, our present results showed that the peak CRP level during hospitalization was significantly associated with the COVID-19 severity. Taking together, these findings further suggest that CRP parallels the severity of tissue injury and is a useful marker for SARS-CoV-2 infection, including the disease severity, response to therapy, and even ultimate recovery.

Other abnormal laboratory findings included depressed lymphocyte counts, increased neutrophil counts and elevated AST levels in SARS-CoV-2 infection. Recently, Qian *et al*. observed that lymphopenia and increased AST were common in SARS-CoV-2 infection [24]. Additionally, Wang *et al*'s study reported that the neutrophil counts continued to increase, while the lymphocyte counts continued to decrease in COVID-19 patients until death occurred [25]. These laboratory abnormalities were similar to those previously reported in MERS-CoV and SARS-CoV infection [26,27], suggesting that severe SARS-CoV-2 infection could lead to cellular immune deficiency, cytokine storm, liver injury and myocardial injury.

Our study has several limitations. First, we did not quantify the viral load in the samples because of the limitation on the method. Considering that viral load is a potential marker associated with disease severity, it should be analyzed in future. Second, COVID-19 diagnosis was only based on the respiratory specimens from the patients suspected of respiratory viral infection. So it might lead to bias in the analysis of clinical features in SARS-CoV-2 infection, especially in those with mild symptoms. Third, this was a retrospective study focusing on the hospitalized patients, and the sample size was relatively small, thus this study may have suffered from selection bias.

Conclusions

Our present study reported that fever and cough were the most common initial symptoms in SARS-CoV-2 infection, and the virus could be efficiently spread by person-to-person transmission. In addition, lymphocyte and neutrophil counts, and serum AST, ALT, CRP and LDH levels were significantly associated

with COVID-19 severity. In order to better prevent and control SARS-CoV-2 transmission, multi-center clinical studies as well as laboratory researches on the characteristics of SARS-CoV-2 infection are still necessary in future.

Abbreviations

SARS-Cov-2: severe acute respiratory syndrome coronavirus-2

COVID-19: Coronavirus disease 2019

ALT: alanine aminotransferase

AST: aspartate aminotransferase

CK: creatine kinase

CRP: C-reactive protein

LDH: lactate dehydrogenase.

Declarations

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Authors' contributions

XL and CD had the original idea, led and wrote the first draft. LW, YZ, YD, YX, YJ, JW and JZ collected and analyzed the data; MY participated in the data analysis. CD drafted the article. All authors approved the final manuscript.

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Availability of data and materials

All data and materials analyzed in this study are available from the corresponding authors on reasonable demands.

Ethics approval and consent to participate

This retrospective study was approved by the Medical Ethical Committee of Huai'an Forth Hospital (approval number HASY2020004) in accordance with the Declaration of Helsinki for Human Research of 1974. A waiver of informed consent was obtained.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

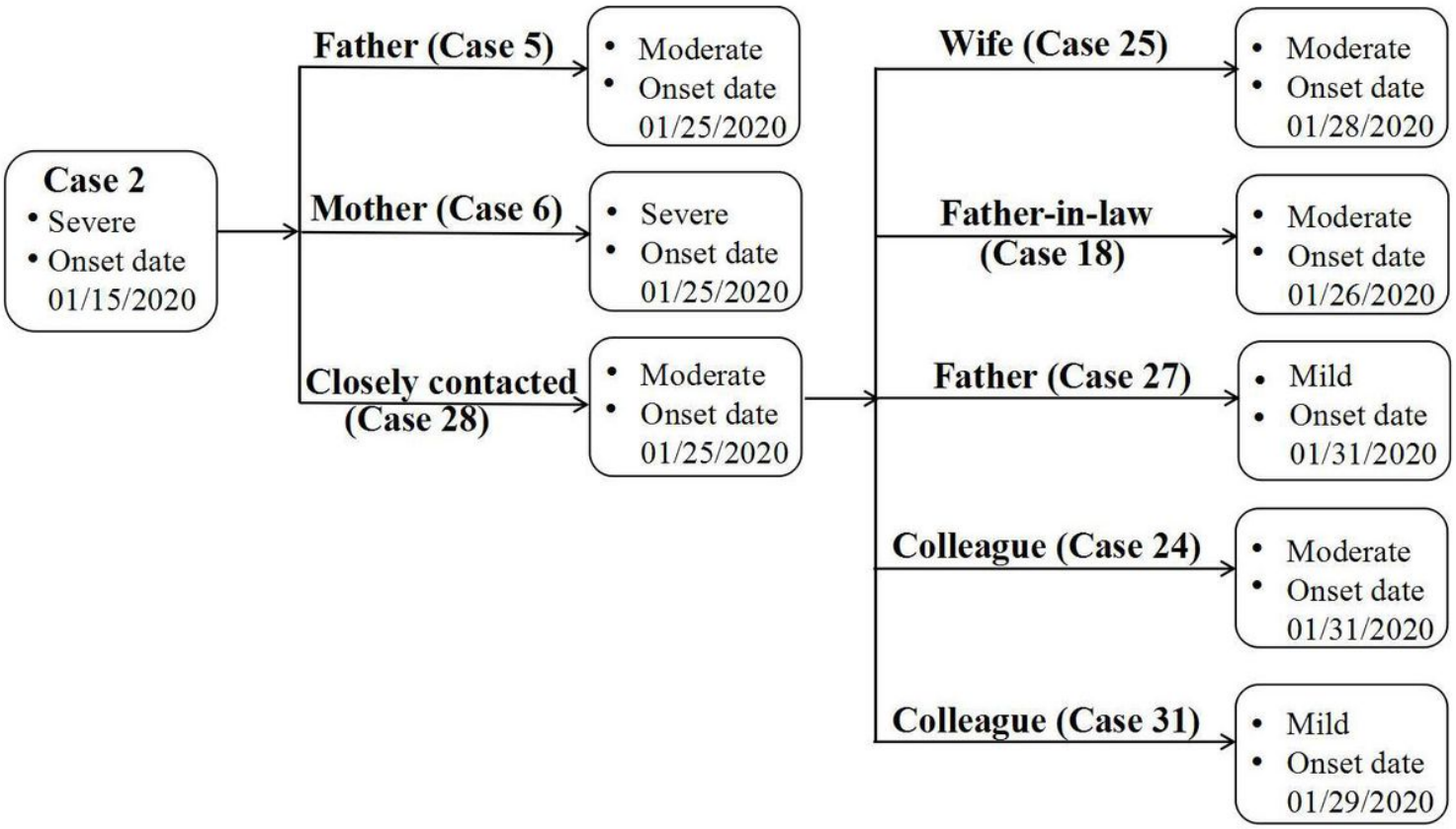

Figure 1

Cluster of nine COVID-19 cases associated with person-to-person transmission