Clinical Characteristics of COVID-19 Pneumonia Patients in Abdoel Moeloek Regional Public Hospital, Bandar Lampung, Indonesia.

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Abstract

a novel coronavirus (SARS-CoV-2) causes a new, really infectious viral disease named COVID-19. This infection quickly develops into a pandemic and it is becoming a major problem in the world. Pneumonia is a severe and dangerous complication of the disease. In this study, we aimed at exploring the clinical characteristics of the COVID-19 pneumonia. A retrospective single-center study in Abdoel Moeloek Hospital of Lampung Province was conducted on March to May 2020. It enrolled 12 Hospitalized patients with confirmed COVID-19 pneumonia by real-time RT-PCR. The purpose of this study was to investigate and describe the features of this epidemic disease. The clinical features, laboratory findings and chest X-ray images of them were reviewed and analyzed. Consecutive patients with COVID-19 pneumonia were included in the study. There were 7 patients who recovered while 5 of them died. Most of them were male (10 patients or 83%) and they were about 40 years (9 patients or 75%). Most of patients (75%) had comorbid disease such as hypertension, diabetes, hepatitis, obesity, and heart disease and they also had a history of travel from infected area. They who died (5 patients or 100%) had comorbid diseases. The patients main complaints were cough and shortness of breath (12 patients or 100%), subfebrile fever (9 patients or 75%), diarrhea (5 patients or 42%), abdominal pain nausea and vomiting (4 patients or 33%). Related to laboratory examination, they got decreasing of calcium level (11 patient or 91%), lymphocytes (9 patients or 75%), hemoglobin level (8 patients or 67%) and albumin levels (7 patients or 58%). On the contrary, they got increasing of the level of the erythrocyte sedimentation rates (12 patients or 100%), the level of C-reactive protein (11 patients or 91%), physiological coagulation (12 patients or 100%), D-dimers plasma levels (10 patients or 83%), liver enzymes test (9 patients or 75%), leukocytes (7 patients or 57%), and chloride (6 patients or 50%). In the chest X-ray interpretations, we found that most of cases (10 patients or 83%) were bilateral pneumonia and they occurred massively in the inferior lobe of the lung. On the death cases, they were found consolidation in both lower lung fields. The clinical data, laboratory and radiological examination of patients with COVID-19 pneumonia showed both inflammation and coagulopathy. A decreased lymphocyte count and plasma calcium level, and an increased high-sensitivity C-reactive protein level and D-dimer plasma level were the most common laboratory findings. The infection caused severe acute respiratory syndrome and it was correlated to high mortality. High efforts are needed for further studies to fulfill the gap in knowledge of this disease.

Key words: COVID-19 pneumonia, clinical manifestation, laboratory findings, chest X-ray, SARS-CoV-2,

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Introduction

The coronavirus disease 2019 (COVID-19) has been declared as a pandemic by the World Health Organisation (WHO). It was caused by the severe acute respiratory syndrome 2 (SARS-CoV-2) virus.[1] It was firstly risen in end of 2019, in Wuhan, Hubei Province, China, and it has spread very quickly. It only took 1 month to escalate from Wuhan Province to the rest of China. Afterwards, the pandemic has spread quickly nationwide to South Korea, Thailand, Japan, and United State of America. Related to this case, more than 200 countries in the world are affected by this pandemic. Even, it causes more than 418.000 death cases, globally. Based on epidemiological data, it indicated person-to-person transmission in community and high infectivity. In fact the COVID-19 is already more widespread than severe acute respiratory syndrome (SARS), it showed more transmissible than previous pandemic .[2]

Furthermore, clinical characteristics of the patients that confirmed to be infected with Covid-19 are similar with two other diseases namely Middle East respiratory syndrome (MERS) and SARS which also caused by coronaviruses, but it revealed more contagious and less virulence if we compared to them, regarding morbidity and mortality.[3,4] Lower respiratory tract illness with low to midgrade fever, dry cough, and dyspnea, and the radiological changes in the lungs are appeared people with COVID-19 pneumonia in early stage. Pneumonia is common complication of COVID-19 .[5]

Thus far, the main treatment concerned to symptomatic support because no antiviral drug with certain effects. Poor treatment efficacy after hospitalization, and developed severe pneumonia, pulmonary edema, acute respiratory distress syndrome (ARDS) or multiple organ failure were performed by some patients.[6] Until now, the treatment of COVID-19 pneumonia is still difficult and complicated. We have to explore it more particularly as concerns mortality. Therefore, we attempted to elucidate the COVID-19 pneumonia patients characteristics in this research.

Methods

This research was a retrospective case-control study. It involved consecutive hospitalized patients with COVID-19 pneumonia in COVID-19 pneumonia isolation ward, Abdoel Moeloek Regional Hospital, Lampung Province, Indonesia. It was carried out from April to May 2020. Hospitalized patients were defined COVID-19 pneumonia according to following criteria: (i) obvious of respiratory symptoms (eg. cough, chest distress and breath shortness); (ii) Respiratory rate ≥20 per min, temperature ≥38 °C, Pulse rate > per 100 min, and crackles were found ; (iii) rapid improvement in lung abnormalities on chest X-ray; (iv) confirmed COVID-19 by SARS-CoV-2 nucleic acid test using real-time reverse-transcription polymerase chain reaction (RT-PCR) of a nasopharyngeal swab. Based on the data by 25 May 2020, 5 of the 12 patients had died, and 7 patients had recovered and they had been discharged. Demographic and clinical data of the patients were obtained from medical records. The data included the following variables: demographic characteristics, comorbidities, clinical symptoms, vital signs, laboratory tests and chest X-ray. Outcomes were also recorded. Categorical variables were presented as numbers and percentages. In addition, continuous variables were displayed as mean or median. The study protocol was approved by ethics committee of the Faculty of Medicine, Universitas Lampung on April 2020.

Results

This study involved 12 patients who had range 25–71 years with COVID-19 pneumonia. They consisted to 7 recovered patients and 5 died patients. Most patients were male (10 patients or 87%) and they were about 40 years old (9 patients or 75%). Almost all of them (9 patients or 75%) had comorbid disease. Four patients had a history of hypertension, two had diabetes, two obesity, one had hepatitis, and one had heart disease. They had a history of travel from outside the province of Lampung or from abroad. Died patients had comorbid diseases (5 patients or 100%). They died less than 10 days of hospitalized. Recovered patients were

hospitalized for more than 20 days. Patient characteristics are detailed in Table I.

Table 1. Characteristics of COVID-19 pneumonia patients in Abdoel Moeloek Regional Public Hospital on April-May 2020. Values are numbers (percentages).

	Total (n=12)	Death (n=5)	Recovered (n=7)
Median age (SD) (years)	52 (13.8)	59 (13.4)	48 (13.6)
< 40 years	3 (25)	1 (20)	2 (29)
40-60 years	6 (50)	2 (40)	4 (57)
>60 years	3 (25)	2 (40)	1 (14)
Sex			
Male	10 (83)	4 (80)	6 (86)
Female	2 (17)	1 (20)	1 (14)
Comorbidities	9 (75)	5 (100)	4 (57)
Hypertension	4 (33)	3 (60)	1 (14)
Obesity	2 (17)	1 (20)	1 (14)
Type II diabetes mellitus	2 (17)	1 (20)	1 (14)
Hepatitis	1 (8)	1 (20)	0
Hearth disease	1 (8)	0	1 (14)
Signs and symptoms at the onset			
Cough	12 (100)	5 (100)	7 (100)
Dyspnea	12 (100)	5 (100)	7 (100)
Fever	9 (75)	5 (100)	4 (57)
Diarrhea	5 (42)	3 (60)	2 (29)
Abdominal pain	4 (33)	1 (20)	3 (43)
Nausea and vomiting	4 (33)	1 (20)	3 (43)
Travel to pandemic area history	12 (100)	5 (100)	7 (100)
Vital sign on admission			
Full of Consciousness	12 (100)	5 (100)	7 (100)
Arterial pressure (mm Hg)			
90-140 mm Hg	8 (67)	2 (40)	6 (86)
≥140 mm Hg	4 (33)	3 (60)	1 (14)
Heart rate ≥ 100 beats/min	7 (58)	3 (60)	3 (42)
Respiration rate			
24-30 breaths per minute	7 (58)	2 (40)	5 (71)
≥30 breaths per minute	5 (42)	3 (60)	2 (29)
Temperature			
36.5-38^{0}C	9 (75)	5 (100)	4 (57)
Percutaneous oxygen saturation ≤93%	12 (100)	5 (100)	7 (100)
Mean hospital admission (days)	16	6	23

Table 1 showed that the median age of died patients was 59 years, which was older than recovered patients (48 years). Most of died patients (4 patients or 80%) were 40

years old or older than it. Men were more predominant in patients who died (4 patients or 80%). All patients (5 patients or 100%) who died had at least one chronic medical condition. In fact, comorbidities were more frequent to died patients (5 patients or 100%) rather than recovered patients (4 patients or 57%).

Furthermore, all of the patients had full of conscious condition on admission. Their main complaints were cough and shortness of breath (12 patients or 100%), subfebrile fever (9 patients or 75%), diarrhea (5 patients or 42%), abdominal pain (4 patients or 33%), nausea and vomiting (4 patients or 33%). On physical examination, they had increasing of respiratory rate and body temperature.

In case of laboratory findings, they got decreasing of calcium level (11 patients or 91%), lymphocytes (9 patients or 75%), hemoglobin level (8 patients or 67%), and serum albumin levels (7 patients or 58%). On the other hand, they got increasing of Erythrocyte sedimentation rates (12 patients or 100%) physiological coagulation (prolonged prothrombin time, 12 patients or 100%), the level of D-dimers (10 patients 83%), the level of C-reactive protein (CRP, 11 patients or 91%), the level of SGOT and SGPT (9 patiens or 75% and 7 patients or 58%, respectively), neutrophil (8 patients or 67%), and leukocytes (7 patients or 58%).

In addition, we noticed that all cases were bilateral pneumonia and they occurred massively in the inferior lobe of the right lung in the chest X-ray interpretations. Moreover, on the death cases, we found consolidation in both lower lung fields.

Discussion

A novel coronavirus (SARS-CoV-2) with unclear origin pneumonia causes a new, highly contagious viral pneumonia namely COVID-19. The viral genome has the ability to access proteins that work effectively and efficiently. There are 29 proteins expressed by this viral genome, and they are divided into two groups namely NSP proteins (labeled with numbers 1 to 16) which function to attack, take over and escape. The second group is SP proteins that work to build the structure of

this virus. If someone inhales a droplet from a COVID-19 patient containing a virus, this virus will get the right habitat to grow and multiply. By using protein S on its surface, this virus will bind to the receptors Angiotensin-converting enzyme 2 (ACE2) found on the surface of the lungs, enterocytes, even in the walls of blood vessels.[7,8] Then, this through this entrance, the virus will infect and damage the lung cells. Coronavirus receptors are not only ACE-2, but it can also be TMPRSS2, Furin and CD147. Specifically for CD147, Coronavirus targets Lymphocytes and Macrophages.[9] After that, the first 256 nucleotides from the SARS-CoV-2 genome will recruit translation devices to translate them into viral proteins. These proteins will fight host cells and they cause cell damages lead to systemic viral sepsis. Next, it can affect systemic inflammatory responds due to Janus Kinase or NF-Kb pathway activation. Then, they can create a dangerous situation called cytokine storm.[10]

12 patients who confirmed COVID-19 pneumonia were involved in this study. Most of the patients were men. Consistent with our study, COVID-19 vulnerability and mortality were seemed to be sex differences to the disease health outcomes. Men tended to be affected by COVID-19 pneumonia and they are usually more refractory than women .[11] It was similar to MERSCoV which were found to infect more men than women.[12] It probably due to gendered differences such as patterns and prevalence of smoking[13], or sex-based immunological.[8] Related to smokers, they are vulnerable to the disease because smoking can upregulate ACE2 receptor, the known receptor for SARS-CoV.[14]

Present study showed that most of the patients and patients who died were about 40 years old. Older age was associated with poor condition and outcome in COVID-19 patients (15). Age $\geqslant$65 years was predictor for mortality of COVID-19 pneumonia patients.[16]

In the case of comorbidities, it was indicated that they were high-risk factors for fatality case COVID-19 pneumonia patients. Consistent with our result, underlying diseases were important risk factors for death of COVID-19 pneumonia.[17] Patients with comorbidities (cardiovascular disease,

diabetes, chronic respiratory disease, hypertension, and cancers) had higher case-fatality rates than those without comorbidities. Most fatal cases were males aged over 50 years with noncommunicable chronic diseases.[16,18,19]

In terms of symptoms, shortness of breath occurred in all patients, The COVID-19 infection has onsets similar to other pneumonias. It can affect multi-organ dysfunction in patients at high risk that caused by pulmonary and systemic inflammation. The most serious complications of covid-19 pneumonia were acute respiratory distress syndrome, respiratory failure, sepsis, acute cardiac injury, and heart failure .[6,20]

Furthermore, in this research, it was found diarrhea in patients as the initial symptom. This finding proposes that gastrointestinal symptoms which is related to the COVID-19 pneumonia pathogenesis as a consequence of the virus binding to human receptor ACE2, which also indicated high expression in the intestine.[21]

The main finding of this study, the patients with COVID-19 pneumonia showed severe inflammation and coagulopathy. Consequently, a declined lymphocyte count and an elevated CRP and D-dimer level were the most susceptible indicators. Lymphopenia was mostly found in deceased patients.[6] The levels of CRP were positively correlated to lung lesion dimensions and severity of disease at the early stage of COVID-19. Its levels could reflect disease severity and should be used as a indicator for patients follow up.[22] Whereas

coagulopathy are indicated by increasing of D-Dimer levels. If they were greater than 2.0 µg/mL (fourfold increase) on admission, they could effectively predict in-hospital mortality in patients with Covid-19.[23] It was consistently reported their gradual increase during disease course was associated with disease worsening. The coagulopathy is a product of the inflammatory response to the infection. Other coagulation abnormalities with severe thrombocytopenia lead to high risk for venous thromboembolism.[24]

Some patients also seem to have thrombosis, as well as an increase in free Fe due to red blood cell lysis. They also show decreased platelets and positive anti-DHF IgM (such as dengue.[25] These various manifestations are due to COVID-19 interacting with many ACE 2 receptors in the lungs and enterocytes, even in the walls of blood vessels .[8]

In this study, we found that there was decreasing of plasma calcium levels in all patients. This is possible because this virus can modulate calcium channels in the host cell. Related to this case, calcium ion is important for viruses to enter the cell and replicate viral genetic material. It also can maturate an entire virus and releasing process. Viruses interfere with calcium pumps or channels in the host cell so that it will change the equilibrium level of the calcium cells of the host cell. Then it modulates the cell signal transduction mechanism according to their will. As a result, beneficial conditions will occur for the development of the virus.[26]

Table 2. Laboratory findings of the patients

	Total (n=12)	Death (n=5)	Recovered (n=7)
Blood routine test			
Low Hemoglobin level (≤130 g/L)	8 (67)	2 (40)	6 (86)
High Leucocyte counts (≥10×10^9/L)	7 (58)	3 (60)	4 (58)
Low Lymphocyte Count (≤1×10^9/L)	9 (75)	5 (100)	4 (57)
High Neutrophil Count (≥6.3×10^9/L)	8 (67)	5 (100)	3 (43)
Normal monocyte Count (0.1-0.6×10^9/L)	8 (67)	5 (100)	3 (43)
Prolonged ESR (≥20mm/hours) Coagulation function	12 (100)	5 (100)	7 (100)
Prolonged Prothrombin time (≥14.5 second)	12 (100)	5 (100)	7 (100)

Normal aPTT (29-42 seconds)	9 (75)	4 (80)	5 (71)
High D-dimer plasma level (≥0.5 µg/L)	10 (83)	5 (100)	5 (71)
Biochemical test			
Low Albumin serum level (≤0.5 g/dl)	7 (58)	2 (40)	5(71)
High AST serum level (≥50 U/L)	9 (75)	5 (100)	4 (57)
High ALT serum level (≥50 U/L)	7(58)	4 (57)	3 (42)
Low Calcium serum level (≤8.8 mg/dl)	11 (91)	4 (80)	7 (100)
Infection			
High C-reactive protein level (≥ 10 mg/dL)	11 (91)	5 (100)	6 (86)
Arterial blood gas analysis			
pH			
Acid (≤7.35)	4 (33)	1 (20)	2 (28)
Neutral (7.35-7.45)	4 (33)	1 (20)	3 (43)
Base (≥7.45)	4 (33)	3 (60)	2 (28)
PaO$_2$, mm Hg			
Low (≤ 80 mm Hg)	6 (50)	4 (80)	2 (28)
Normal (80-108 mm Hg)	3 (50)	1 (20)	2 (28)
High (≥ 108 mm Hg)	3 (50)	0 (0)	3 (43)
PaCO2, mm Hg			
Low (≤ 35 mm Hg)	10 (83)	5 (100)	5 (71)
Normal (35-45 mm Hg)	2 (17)	(0)	2 (29)
HCO$_3^-$			
Low (≤ 23 mmol/L)	9 (75)	5 (100)	4 (57)
Normal 23-29 mmol/L	3 (25)	(0)	3 (43)

ERS=Erythrocyte sedimentation rate
AST=Alanine Aminotransferase
ALT =Aspartate aminotransferase
aPTT = Activated partial thromboplastin time

The current study indicated that 9 of 12 patients COVID-19 pneumonia (75 %) had abnormal liver tests. In line to our research, most of covid-19 patients will get abnormal liver test. They will also have significantly higher odds of developing severe pneumonia and few of them have liver injury in the course of hospitalization .[27] There are three following causes that can affect liver injury in COVID-19 patients. They are related to several drugs used during medical treatment, directly

liver injury by hepatocyte viral infection and immune-mediated inflammation.[27,28,29] In our study, we highlight that liver injury in patients might be caused by hepatocyte Covid-19 infection because they got increasing of liver function test at admission.

Moreover we found that all cases were bilateral pneumonia mostly massive occurred in the inferior lobe of the right lung in the chest X-ray analyzing. In line with our findings, other research showed that the most prevalent chest X-ray imaging for covid-19 pneumonia were identified as an interstitial and/or multifocal pattern and it involved the lower lobes.[30] It can be affected by anatomical characteristic of the right inferior lobar bronchus. There is steeper and straighter bronchus of the right lower lobe of the lung rather than other branches, and it also has narrower size of the angle between the right lower lobe and the long axis of the trachea. Therefore the virus is more likely to attack the branches of the right inferior lobar bronchus and it causes infection in the untimely phase of the infection. By considering the involvement range, a lesion predominantly peripheral distribution were found.[31]

Table 3. Chest X-ray findings of the patients

	Total (n=12)	Death (n=5)	Recovered (n=7)
Bilateral pneumonia	10 (83)	5 (100)	5 (71)
Consolidation	7 (58)	3 (60)	4 (57)
Distribution			
Right lung	3	0	3
Left lung	1	1	0
Bilateral	8	4	4
Upper zone predominant	0	0	0
Lower zone predominant	8	5	3
No zonal predominance	4	0	4
Pleural effusion	0	0	0
Cardiomegaly	6 (50)	1 (20)	5 (71)

Radiological abnormalities in COVID-19 pneumonia can be detected by chest X-ray or CT scan. Chest x-ray abnormalities in COVID-19 have some similarities with CT-scan which can show bilateral peripheral consolidation. Chest X-ray findings have a lower sensitivity than CT-scan. On the other hand, it can be the primary imaging modality used in diagnosis and management of COVID-19 patients. It has a low-cost, widely available equipment, quick, and effective in detecting lung abnormalities in COVID-19 pneumonia patients.[32,33] However, it will be likely the most commonly applied tool for identifying and following up of lung abnormalities due to infection control issues and lack of CT availability in some countries.[34]
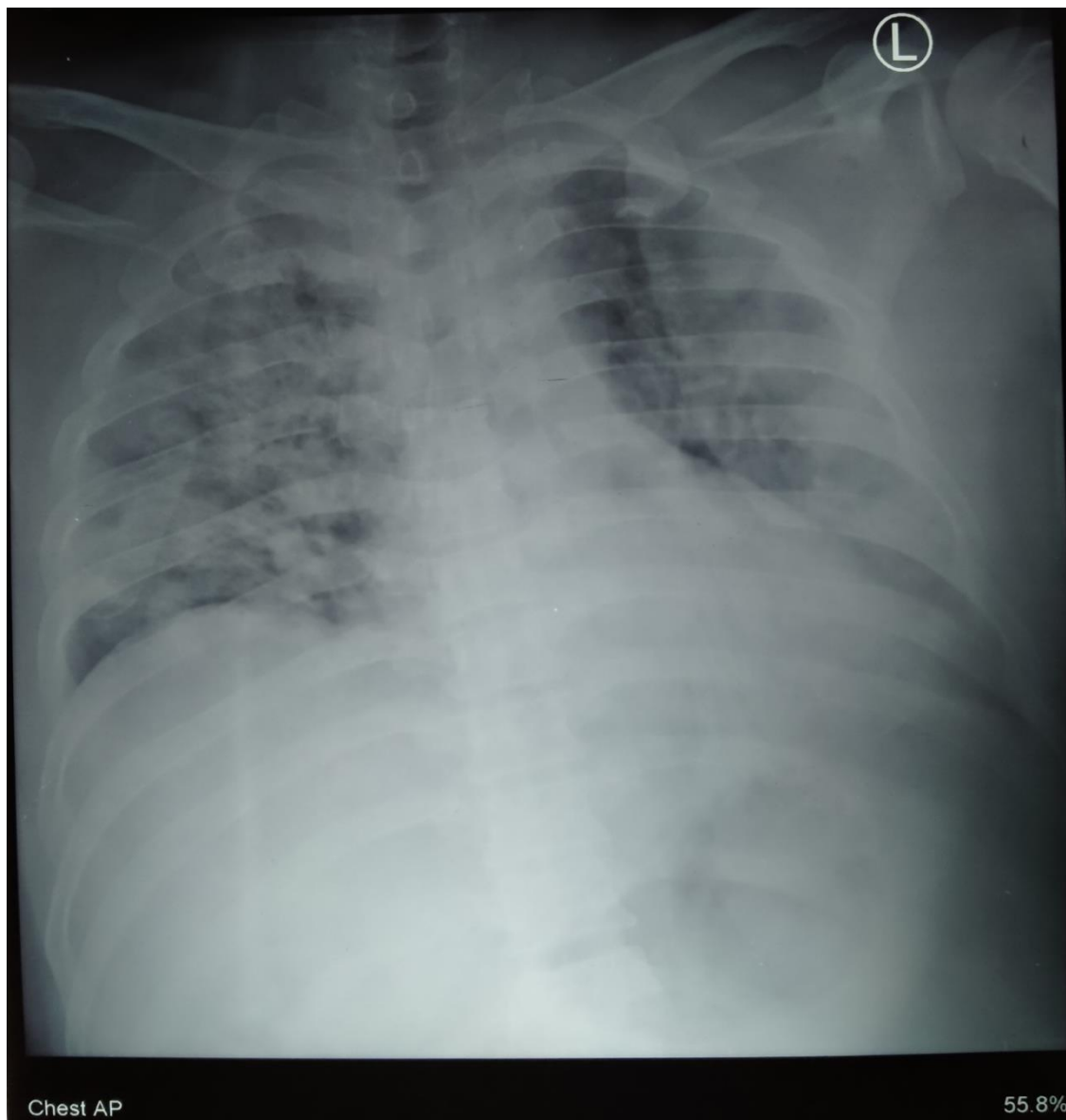
Grapich 1. This is a Chest x-Ray Posteroranterior view of Covid-19 pneumonia death patient. He was 50 years old who had obesity. Chest radiograph showed bilateral peripheral opacities with crazy paving pattern.

There are two limitations in this current research. Firstly, the number of sample was very small. Secondly, changes seen on laboratory examination and chest X-ray over its whole course had not been wholly documented and they did not represent for all patients because the course of COVID-19 pneumonia was brief. Thirdly, there was not sufficient pathologic data on these patients such as a limitation of CT-scan facilities in our center for a comparative study to be employed.

Conclusions

We conclude that clinical findings for patients with COVID-19 pneumonia indicated that it had a combination both lung inflammation and blood coagulopathy. The most common laboratory findings were a decline of lymphocyte count, an increased CRP level,

and a bilateral pneumonia. We need larger multi-centered studies to find out the clinical manifestations of the disease.

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