An Analysis on the Clinical Features of MHD Patients with Coronavirus Disease 2019: A Single Center Study

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Research article

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Abstract

Background: In this study, we aimed to find out the features of the maintenance hemodialysis (MHD) patients infected with Coronavirus Disease 2019 (COVID-19) in the Blood Purification Center of Wuhan No.1 Hospital, Hubei Province, China, and provide evidences for clinical treatment.

Methods: We collected the data of all the MHD patients in this hemodialysis center by February 20, 2020, including those infected with COVID-19. These patients were divided into three groups: the control group (537 cases), confirmed group (66 cases) and suspected group (24 cases). We compared the relevant data of the three groups and analyzed the factors that may affect the possibility of catching COVID-19.

Results: 1. By February 20, 2020, there were 627 MHD patients in the Hemodialysis Center of Wuhan No.1 Hospital. The prevalence rate of the COVID-19 was 14.35% (90/627, including 66 confirmed cases and 24 suspected cases); the fatality rate 13.33% (12/90, including 12 death cases); the mortality rate 1.91% (12/627).**2.** The comparison between the three groups revealed the following results: weekly hemodialysis duration (WHD), ultrafiltration volume (UFV) and ultrafiltration rate (UFR) of the confirmed group were obviously lower than those of the control and suspected groups (P<0.05); the neutrophil ratio (N%), neutrophil (N#), monocyte (M#) and total carbon dioxide (TCO_2) were significantly higher than those of the control group while the lymphocyte ratio (L%) was much lower (P<0.05).**3.** The lung CT scans found three common features: bilateral abnormalities (81.54%), multiple abnormalities (84.62%) and patchy opacity (61.54%).**4.** The binary logstic regression analysis showed that diabetes (*OR*=5.404,95% *CI* 1.950–14.976, *P*=0.001) and hypertension (*OR*=3.099,95% *CI* 1.380–6.963, *P*=0.006) are independent risk factors for MHD patients to be infected with COVID-19; WHD (*OR*=0.846,95% *CI* 0.737–0.970, *P*=0.017), UFR (*OR*=0.012,95% *CI* 0.002–0.058, *P*<0.001) and serum ferritin (SF, *OR*=0.823,95% *CI* 0.748–0.906, *P*<0.001) are independent protective factors.

Conclusion: MHD patients with diabetes or hypertension are more likely to be infected with COVID-19. In clinical treatment, hemodialysis duration, UFR and SF levels should be controlled appropriately to reduce the risk of infection.

Background

In December 2019, a series of pneumonia cases of unknown cause emerged in Wuhan, Hubei Province, China[1]. A novel coronavirus was subsequently identified as the causative pathogen, provisionally named 2019 novel coronavirus (2019-nCoV)[2, 3]. This is a high-infectivity coronavirus that transmits quickly and mainly through droplet and contact. The clinical manifestations of the pneumonia include fever, fatigue, dry cough, gradually developing into dyspnea. Most of the patients have a good prognosis while some patients may develop acute respiratory distress syndrome or septic shock, or even die. New infected cases are still increasing. As we all know, hemodialysis (HD) patients tend to suffer from low immunity and complications like cardiovascular diseases and diabetes. Since HD patients need to go to hospital frequently, they are more likely to be attacked by the 2019-nCoV. Additionally, the crowded and closed

space in the hemodialysis room also increase the possibility for HD patients to be infected. The research aims to describe the clinical features of MHD patients infected with COVID-19, find out the risk factors of the infection, and provide evidence for reducing the incidence of COVID-19.

Methods

Research Objects

In this single center study, all data are from the HIS system of Wuhan No.1 Hospital and all the patients have taken 2019-nCoV nucleic acid detection with their pharynx or nasal swab samples and / or had lung CT scanning.

Methods

1. **Data Collection**

General information, hemodialysis indicators and laboratory indexes of the patients were collected. The general information includes gender, age, clinical features and primary disease. Hemodialysis indicators contain hemodialysis age, WHD, types of vascular access, dry weight (DW), UFV, UFR, dehydration rate (DR), systolic blood pressure (SBP) and diastolic blood pressure (DBP). Laboratory indexes include white blood cell (WBC), red blood cells (RBC), hemoglobin (Hb), platelets (PLT), neutrophil ratio (N%), neutrophil (N#), lymphocyte ratio (L%), lymphocyte (L#), monocyte percentage (M%), monocyte (M#), glutamic pyruvic transaminase (GPT), glutamic oxaloacetic transaminase (GOT), total protein (TP), albumin (ALB), γ-glutamyl transpeptidase (γ-GT), urine nitrogen (BUN), creatinine (Cr), total carbon dioxide ($TCO_{2)}$, uric acid (UA), kalium (K), calcium (Ca), phosphorus (P), serum ferritin (SF), parathyroid hormone (PTH), c-reactive protein (CRP), erythrocyte sedimentation rate (ESR), procalcitonin (PCT) and lactate dehydrogenase (LDH).

2. **Diagnostic Criteria**

This research used the diagnostic criteria specified in the *Diagnosis and Treatment Planning of the Novel Coronavirus Pneumonia (the Sixth Trial Edition)*[4] jointly published by the National Health Commission (NHC) and National Administration of Chinese Traditional Medicine. All MHD patients in the Hemodialysis Center were divided into three groups: control group, suspected group and confirmed group.

3. **Statistical Methods**

Software SPSS 22.0 is used to perform statistical analysis. The measurement data presenting normal distribution are expressed by (± s), while that presenting skew distribution are expressed by median and interquartile range, i.e. M (P_{25}, P_{75}). Count data are demonstrated in n (%). Measurement data displaying normal distribution are compared between groups with analysis of variance, while that displaying skew distribution are compared between groups through Mann-Whitney U test. Multiple-group analysis is performed through Kruskal-Wallis test. Counting data are compared by χ^2 test. Binary logstic regression is

used to analyze the risk factors for MHD patients to be infected with COVID-19. $P < 0.05$ means that the difference is statistically significant.

Results

By February 20, 2020, there were 627 MHD patients in the Hemodialysis Center of Wuhan No.1 Hospital, among which 66 patients (73.33%) were identified as infected with COVID-19, 24 were suspected cases (26.67%) and 12 died of the novel coronavirus (1.91%). The case fatality rate recorded 13.33%. In all the COVID-19 infected cases (including both confirmed and suspected cases), 40 cases were male (44.44%) and 50 female (55.56%), aged 61.34 ± 12.59. Primary diseases included 34 primary glomerulonephritis cases (37.78%), 16 diabetic nephropathy cases (17.78%), 24 hypertensive nephropathy cases (26.67%), 4 lupus nephritis cases (4.44%) and 12 other diseases (13.33%). In terms of the first symptoms, asymptomatic patients accounted for 26% while symptomatic patients most commonly presented dry cough (36%), followed by fatigue (16%), dyspnea (16%), fever (13%), poor appetite (4%), diarrhea (2%) and nausea (1%). COVID-19 infected patients mainly resided in Qiaokou District (29.89%), Jianghan District (16.67%) and Hanyang District (15.56%). (Table 1 and Fig.1)

A comparison between the hemodialysis indicators of the three groups showed the WHD, UFV and UFR of the confirmed group were significantly lower than those in the control and suspected group (P□0.05). (Table 2)

A comparison between the laboratory indexes of the three groups revealed that the N%, N#, M#, and TCO_2 of the confirmed group were significantly higher than the control group, and that of L% much lower than the control group (P□0.05). (Table 3)

The lung CT scans of 65 suspected and confirmed patients were collected. Among these patients, 12 cases presented abnormalities in single lung (18.46%), while 53 cases presented abnormalities in two lungs (81.54%); 10 cases displayed solitary abnormality (15.38%) while 55 cases displayed multiple abnormalities (84.62%); 40 cases displayed patchy opacity (61.54%), 23 cases ground-glass opacity (35.38%) and 2 cases patchy ground-glass opacity (3.08%). (Fig. 2; 3; 4; 5)

A binary logstic regression was used to analyze the risk factors for MHD patients to be infected with NCP (confirmed cases). The binary logstic regression was applied to analyze the data collected in this research and the forward stepwise regression was adopted in multi-factor analysis. The results showed that diabetes (*OR*=5.404,95%*CI* 1.950□14.976, *P*=0.001), hypertension (*OR*=3.099,95%*CI* 1.380□6.963, *P*=0.006), Procalcitonin (PCT) (*OR*=1.181,95%*CI* 1.028□1.355, *P*=0.018) and TCO_2 (*OR*=1.121,95%*CI* 1.009 □1.245, *P*=0.033) constitute independent risk factors for MHD patients to be infected with COVID-19; and WHD (*OR*=0.846,95%*CI* 0.737□0.970, *P*=0.017), UFR (*OR*=0.012,95%*CI* 0.002□0.058, *P*□0.001) and serum ferritin (SF) (*OR*=0.823,95%*CI* 0.748□0.906, *P*□0.001) are independent protective factors. (Table 4)

Discussion

Existing studies indicated about half of COVID-19 patients (51%) also suffer from a number of chronic diseases[5], among which chronic kidney disease (CKD) is one of the common diseases. CKD claims a prevalence rate of 10.8% in China's adult population and currently around 120 million CKD patients live in China[6].This gives rise to the increasing demand of renal replacement therapy. It is estimated the incidence of HD reached 402.18 per million population in China[7], while the pneumonia incidence of MHD patients is 14~16 times of ordinary people[8]. Therefore, MHD patients are one of the susceptible populations of COVID-19 and require high attention.

Results of this research revealed that the prevalence rate at our Hemodialysis Center was 14.35% while the case fatality rate reached 13.33%, higher than the results of single-center research by Wuhan Jinyintan Hospital[5] and significantly higher than the national total CFR (2.3%)[9]. MHD patients tend to suffer from multiple basic diseases, including hypertension, diabetes and coronary heart disease, and are susceptible to anemia, hypoalbuminemia, hyperphosphatemia and other factors that may increase death risk. The attack of the 2019-nCoV on their already weak immune system could be fatal. In this study, the primary diseases of COVID-19 patients included primary glomerulonephritis (37.78%), hypertension (26.67%) and diabetes (17.78%), a combination slightly different from other studies that surveyed patient groups with primary diseases of diabetes (20%), hypertension (15%) and cardiovascular diseases (15%) [1]. Logstic regression analysis revealed that hypertension and diabetes are among the independent risk factors of COVID-19. Therefore, more importance should be attached to controlling the primary diseases like hypertension and diabetes on MHD patients. COVID-19 patients in this research have an average age of 61.34 years old, older than that of similar studies (55.5 years old) [5], which might accounted for the higher mortality rate in this study. In addition, the most common clinical manifestations for COVID-19 patients in this study are cough (36%), followed by fatigue(16%) and dyspnea (16%), which is slightly different from other studies that reported fever as the main symptom[1, 5]. Besides, this study found the majority of MHD patients (26%) displayed no clinical manifestations, similar to the results of certain studies [10]. This would significantly increase the difficulty to screen COVID-19 patients. Therefore, measures should be taken in the clinical aspect to reinforce the screening of COVID-19 on MHD patients.

Meanwhile, this study revealed the WHD, UFR and UFV of the confirmed group were much lower than those of the control and suspected group. This indicates that MHD patients infected with COVID-19 might have received inadequate hemodialysis that didn't remove the excessive toxins and water from the patients, thus giving rise to a series of complications including the retention of water and sodium, electrolyte disturbance and malnutrition, increasing death risk. Moreover, though the confirmed group had a TCO_2 level falling within the normal range, its level was higher than that in the other two groups. The mechanisms behind the high TCO_2 level in the confirmed group remain unclear and require further research. The logstic regression analysis of this study revealed that the WHD, UFR and TCO_2 are the independent risk factors of COVID-19 infection. This offers the enlightenment that during the outbreak of the COVID-19, measures should be taken to lengthen hemodialysis durations for MHD patients and appropriately increase UFR, ensuring the adequacy of hemodialysis to decrease the amount of CO_2 and

lower the risk of infection. The laboratory indexes revealed that the L% of the confirmed group was significantly lower than that of the control group, which is consistent with the results of similar studies [1, 9, 10]. The fact that the N%, N# and M# of the confirmed group were much higher than the control group indicates that MHD patients may also suffer from bacterial infection when they were infected with 2019-nCoV. Therefore, based on the patient's condition, anti-bacterium therapies might be given to MHD patients infected with COVID-19 along with anti-virus therapies. Surveyed COVID-19 patients in his study presented in their lung CT scans common features of bilateral abnormalities, multiple abnormalities and patchy opacity. In comparison, relevant diagnostic guidelines[4, 11] pointed out that COVID-19 in early stage presented the imaging features of multiple small patchy opacity or interstitial changes, followed by bilateral multiple ground-glass opacity and even pulmonary consolidation in severe cases. In this regard, screening work should be conducted in time on the lung CT scans of MHD patients to achieve early detection of the disease and put the patients in quarantine and in treatment as early as possible. Xin Fang et al [12] found that the COVID-19 might rebound and exacerbate the conditions of patients in the recovery stage. This also proves the key role lung CT scan plays in diagnosing COVID-19 in testing and locating the abnormalities and keeping dynamic observations, especially in circumstances where nucleic acid detection presents low sensitivity.

In conclusion, considering that this is a horizontal research, further longitudinal research might be required to discuss other complexities of COVID-19. Secondly, given the insufficiency and low sensitivity of 2019-nCoV nucleic acid detection reagent at the early phase of the epidemic, some MHD patients infected with COVID-19 were diagnosed solely on the basis of clinical manifestations, hemanalysis and lung CT scans, which might affect the results to some extent. Also, this Hemodialysis Center only offers ambulatory hemodialysis and COVID-19 screening services. All confirmed patients were required by the government to be transferred to designated hospitals to receive treatment. This also constituted an imperfection in the results. Lastly, this is a single-center study supported by a relatively small number of samples, meaning that further multi-center studies of larger sample size are imperative to consolidate the conclusions of this study.

Conclusion

Our study showed that among MHD patients infected with COVID-19, female patients constitute the majority. Most infected patients reside at Qiaokou District, Wuhan City, a short distance from South China Seafood Wholesale Market, the epicenter of the 2019-nCoV outbreak. The proportion of asymptomatic HD patients in the total can hardly be ignored. In light of these findings, this article suggests dynamic monitoring be carried out on MHD patients with latent COVID-19 infection, such as having temperature and SpO_2 tests at the waiting area before HD treatment, re-examining blood routine, lung CT scans and nucleic acid detection of 2019-nCoV on a regular basis, and arranging confirmed patients in quarantined spaces and non-confirmed patients in separate spaces for hemodialysis. In addition, hemodialysis schedules need adjusting to proactively prevent complications for patients who also suffer from hypertension, diabetes or receive inadequate hemodialysis. Our research found out that the levels of

TCO_2, PCT and SF have certain effects on controlling COVID-19. Keeping these indicators within normal ranges may effectively lower the risk of infection.

It's worth noting that COVID-19 broke out in Wuhan, China, a city home to about 7,000 people in need of hemodialysis. Up to present, we have found no study has been published on the clinical features of MHD patients infected with 2019-nCoV. This article seeks to provide evidences for the clinical prevention and treatment of COVID-19.

List Of Abbreviations

MHD：aintenance hemodialysis

COVID-19：Corona Virus Disease 2019

2019-nCoV：2019-new coronavirus

HD：Hemodialysis

WBC：White blood cell

RBC：Red blood cells

Hb：Hemoglobin

PLT：Platelets

N%：Neutrophil ratio

N#：Neutrophil

L%：Lymphocyte ratio

L#：Lymphocyte

M%：Monocyte percentage

M#：Monocyte

GPT：Glutamic pyruvic transaminase

GOT：Glutamic oxaloacetic transaminase

TP：Total protein

ALB：Albumin

γ-GT：γ-glutamyl transpeptidase

BUN：Urine nitrogen

Cr：Creatinine

TCO2：Total carbon dioxide

UA：Uric acid

K：Kalium

Ca：Calcium

P：Phosphorus

SF：Serum ferritin

PTH：Parathyroid hormone

CRP：C-reactive protein

ESR：Erythrocyte sedimentation rate

PCT：Procalcitonin

LDH：Lactate dehydrogenase

CKD：Chronic Kidney Disease

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Wuhan NO.1 Hospital . Due to the retrospective nature of the study,the need for informed consent was waived

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are available from corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors Contributions

CL and MYl designed the study. CL, MYl, TC, MDd collected the data and analyzed it statistically. CLand MYl wrote the text. LHf provided CT pictures and XF reviewed and revised the article. All authors have read and approved the manuscript.

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Tables

Table 1
Description of the Patients

	N=90
2019-nCoV Patients (cases/%)	
Confirmed	66/73.33%
Suspected	24/26.67%
Gender (cases/%)	
Male	40/44.44%
Female	50/55.56%
Age (years old)	61.34±12.59
Clinical Features (cases/%)	
Asymptomatic	23/26%
Fever	11/13%
Fatigue	14/16%
Dry Cough	32/36%
Poor Appetite	4/4%
Nausea	1/1%
Diarrhea	2/2%
Dyspnea	14/16%
Primary Diseases (cases/%)	
Primary Glomerulonephritis	34/37.78%
Diabetic Nephropathy	16/17.78%
Hypertensive Nephropathy	24/26.67%
Lupus Nephritis	4/4.44%
Others	12/13.33%
Prevalence Rate (%)	14.35%
Case Fatality Rate (%)	13.33%
Mortality Rate (%)	1.91%

Proportions are depicted as number of patients, with percentages in brackets, n(%)
The normal distribution is expressed by (x±s)

Table 2
Comparison of Hemodialysis Indicators in Three Groups

Indicators	Control Group n=537	Suspected Group n=24	Confirmed Group n=66	F/Z/χ2	P
Hemodialysis Age	62（39,94）	68（36,98）	57（36,71）	0.605	0.739
WHD (hours/week)	10.12±2.57	10.52±2.08	9.22±2.09ab	4.186	0.016
Vascular Access					
AVF	424（79.0）	18（75.0）	46（69.7）	3.037	0.219
Non-AVF	113（21.0）	6（25.0）	20（30.3）		
DW（kg）	59.58±12.61	62.74±17.07	59.03±11.20	0.744	0.476
UFV（kg）	2.16±0.82	2.33±0.89	1.64±0.76ab	10.610	<0.001
UFR	0.79±0.27	0.83±0.33	0.61±0.28ab	8.648	<0.001
DR	1.37±0.11	1.38±0.10	1.35±0.07	1.070	0.344
SBP（mmHg）	147.4±21.88	151.26±23.46	145.46±29.57	0.508	0.620
DBP（mmHg）	79.80±12.71	80.39±16.29	76.71±14.52	1.276	0.280

The normal distribution is expressed by (x±s)；The skew distribution are expressed by M (P25, P75).
“a” suggests when compared with the control group, P<0.05; “b” suggests when compared with the suspected group, P<0.05.
WHD: weekly hemodialysis duration; AVF: arteriovenous fistula; DW: dry weight; UFV: ultrafiltration volume; UFR: ultrafiltration rate; DR: dehydration rate; SBP: systolic blood pressure; DBP: diastolic blood pressure.

Table 3
Comparison of Laboratory Indexes in Three Groups

Indexes	Control Group n=537	Suspected Group n=24	Confirmed Group n=66	F/Z/χ2	P
WBC（10^9/L)	6.06±2.69	6.37±1.81	6.50±3.35	0.751	0.472
RBC (10^12/L)	3.53±0.66	3.82±1.14	3.50±0.66	1.897	0.151
Hb （g/L)	103.02±17.41	99.08±18.95	101.29±17.54	0.812	0.445
PLT (10^9/L)	166.10±61.65	192.33±61.08	160.43±79.02	2.283	0.103
N%(%)	69.63±9.29	72.10±8.02	72.81±9.73a	3.997	0.019
N# (10^9/L)	4.19±1.94	4.66±1.35	4.82±3.11a	3.139	0.044
L%(%)	18.80±6.87	17.17±5.83	16.56±7.28a	3.554	0.029
L# (10^9/L)	1.05±0.42	1.13±0.50	0.95±0.41	2.293	0.102
M%(%)	6.96±2.69	6.72±2.88	7.76±3.19	2.635	0.073
M# (10^9/L)	0.40±0.18	0.43±0.20	0.46±0.20a	3.728	0.025
CRP (mg/L)	5.28 （3.23,21.75）	6.52 （3.23,82.65）	6.98 （3.23,34.80）	0.735	0.693
ESR (mm/h)	25.00 （46.00,75.00）	81.00（55.50,102.00）	53.50 （22.50,85.75）	3.434	0.180
GPT (U/L)	9.00 （6.00,13.00）	8.00 （6.00,14.00）	10.00 （6.00,13.00）	0.092	0.955
GOT (U/L)	14.00 （11.00,18.00）	13.00（10.0,17.00）	13.00 （11.50,20.00）	0.276	0.871
TP (g/L)	64.63±6.10	64.73±4.91	65.06±6.09	0.146	0.864
ALB (g/L)	38.71±3.87	37.32±6.72	38.54±4.38	1.304	0.272
γ-GT (U/L)	16.00 （12.00，29.00）	19.00 （13.00,52.00）	20.00 （14.00,32.00）	4.248	0.120
PCT (ug/L)	0.40（0.19,1.27）	0.77（0.26,5.43）	0.59（0.31,1.24）	2.684	0.261
LDH (U/L)	183.17±59.12	169.92±40.45	184.60±51.96	0.344	0.709
BUN (mmol/L)	17.43±8.83	18.05±10.18	16.33±8.70	0.524	0.592
Cr (μmol/L)	710.17±337.12	667.83±355.32	694.65±321.22	0.223	0.800
TCO_2 (mmol/L)	22.91±3.48	23.01±3.61	24.10±3.145a	3.375	0.035
UA (mmol/L)	313.87±160.92	348.35±182.54	300.15±156.80	0.760	0.468
K (mmol/L)	4.54±0.87	4.47±1.11	4.52±0.89	0.094	0.910
Ca (mmol/L)	2.15±0.27	2.10±0.20	2.16±0.28	0.503	0.605
P (mmol/L)	1.67±0.55	1.78±0.79	1.66±0.59	0.461	0.631
PTH (pg/ml)	322.65 （159.05,322.65）	295.80（108.25,500.88）	242.60 （117.83,465.35）	5.841	0.054
SF (μmol/L)	12.55±7.84	11.17±3.82	8.16±4.29	1.622	0.201

The normal distribution is expressed by (x±s)，The skew distribution are expressed by M (P25, P75).
“a” suggests when compared with the control group, P＜0.05.
WBC: white blood cells; RBC: red blood cells; Hb: hemoglobin; PLT: platelets; N%: neutrophil ratio; N#: neutrophil; L%: lymphocyte ratio; L#: lymphocyte; M%: monocyte percentage; M#: monocyte; GPT: glutamic pyruvic transaminase; GOT: glutamic oxaloacetic transaminase; TP: total protein; ALB: albumin; γ-GT: γ-glutamyl transpeptidase; PCT: procalcitonin; LDH: lactate; BUN: blood urine nitrogen; Cr: creatinine; TCO2: total carbon dioxide, UA: uric acid; K: kalium ; Ca: calcium; P: phosphorus; PTH: parathyroid hormone; CRP: c-reactive protein; ESR: erythrocyte sedimentation rate; SF: serum ferritin.

Table 4 Analysis of Risk Factors for MHD Patients Infected with the COVID-19

Risk Factors	OR	95%CI	P
Diabetes	5.404	1.950□14.976	0.001
Hypertension	3.099	1.380□6.963	0.006
WHD	0.846	0.737□0.970	0.017
UFR	0.012	0.002□0.058	□0.001
PCT	1.181	1.028□1.355	0.018
TCO2	1.121	1.009□1.245	0.033
SF	0.823	0.748□0.906	□0.001

Confirmed Case = 1, Non-confirmed Case = 0; Diabetes = 1, Non-diabetes = 0; Hypertension = 1, Non-hypertension = 0.

Figures

Figure 1

The Distribution of Patients' Residence Places (patients/%). Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

Figure 2

Bilateral patchy ground-glass opacity

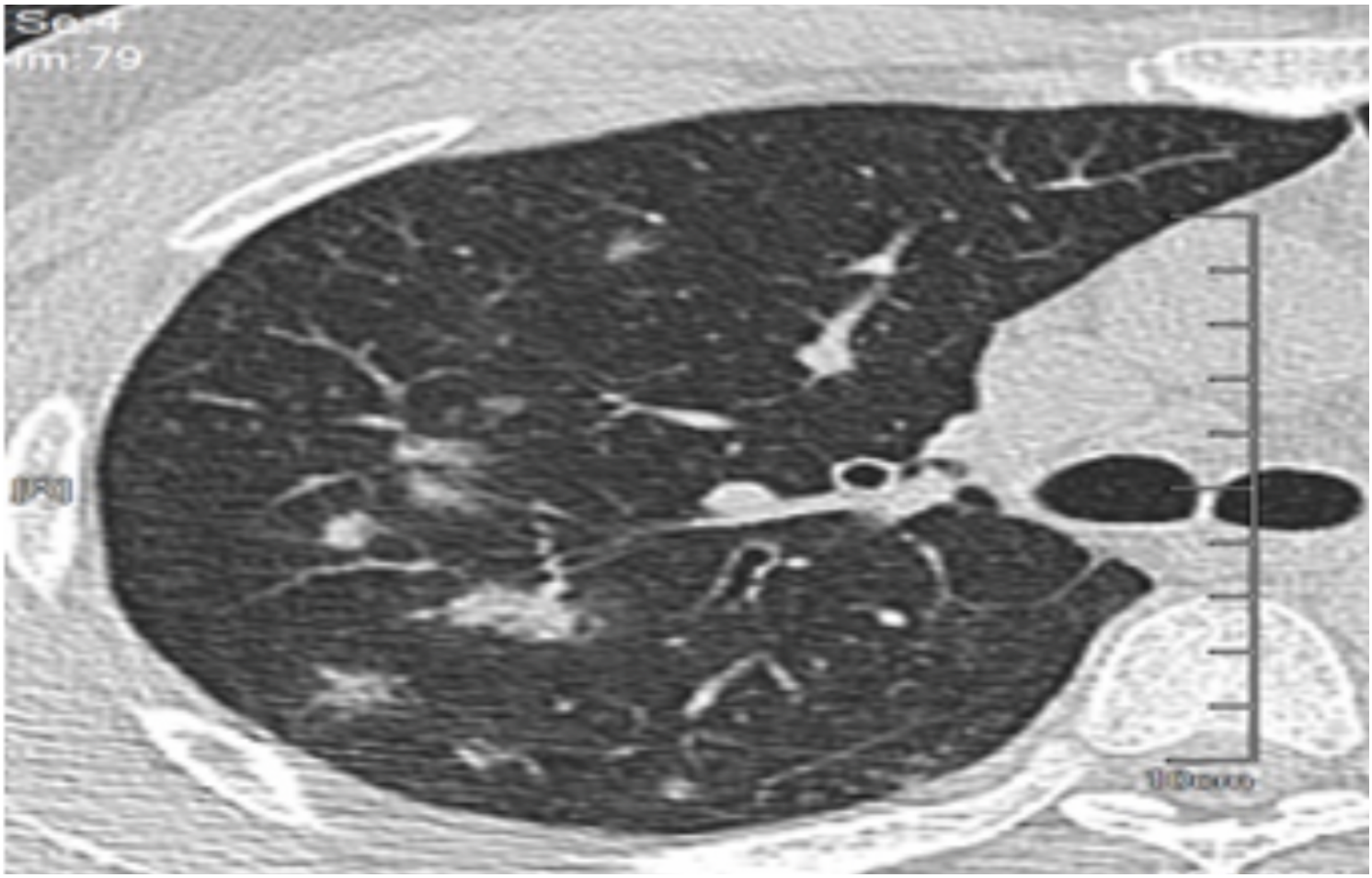

Figure 3

Right lung multiple small patchy ground-glass opacity

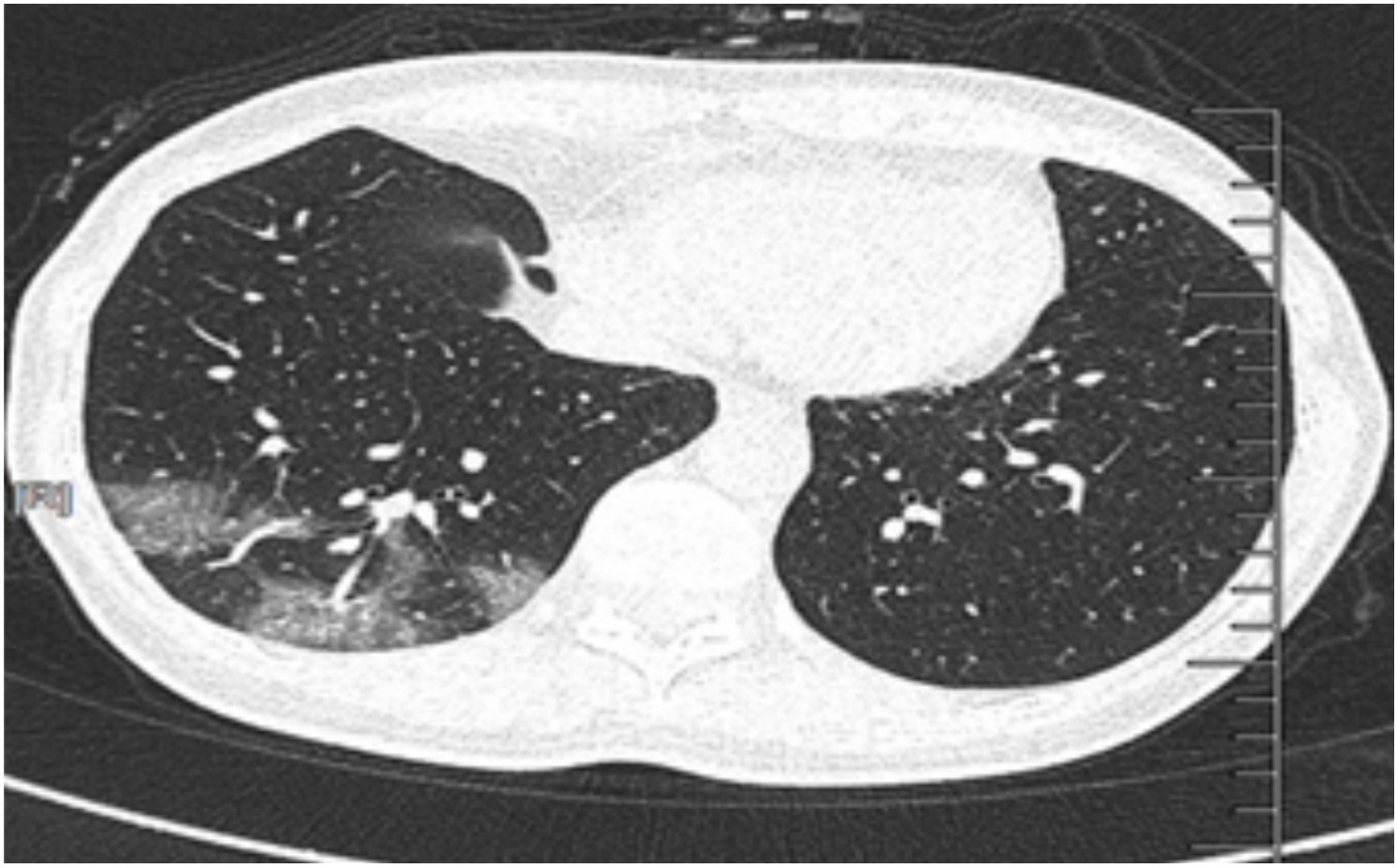

Figure 4

Multiple patchy ground-glass opacity right lower lobe

Figure 5

Solitary ground-glass opacity in right lower lobe