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Pleural effusion as an indicator for the poor prognosis of COVID-19 patients

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Abstract

Background: Coronavirus Disease 19 (COVID-19) is a global health concern that has become a pandemic over the past few months. This study aims at understanding the clinical manifestations of COVID-19 patients with pleural effusion.

Methods: COVID-19 patients were retrospectively enrolled from the Union Hospital, Tongji Medical College, Huazhong University of Science and Technology. Pharyngeal swabs from patients were tested using real-time polymerase chain reaction. Patients with COVID-19 were divided into two groups based on their computed tomography (CT) scans for the presence of pleural effusion at admission. We compared the clinical features, laboratory findings, scans and clinical outcomes between the two groups.

Results: Pleural effusion was observed in 9.19% of the patients. Patients with pleural effusion were more likely to be severe or critical cases. Moreover, patients with pleural effusion were associated with increased mortality. Of the 799 discharged patients, patients with pleural effusion had longer hospital stays and duration of viral shedding since the onset of symptoms as compared with that for patients without pleural effusion. After discharge, 217 patients visited for a follow-up CT re-examination at the Union Hospital. The CT scans showed that patients with pleural effusion required a longer time to resolve the lung inflammation after the onset of COVID-19 as compared with the time required by patients without pleural effusion.

Conclusion: This population of patients requires special attention and pleural effusion may be an indicator of poor prognosis in COVID-19 patients.

1 | INTRODUCTION

Coronavirus Disease 2019 (COVID-19), caused by the novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), has become a pandemic since its outbreak in Wuhan, China in late December, 2019. As of 14 July 2020, the World Health Organization has reported 12,964,809 infected individuals and 570,288 deaths globally.[1] Thus, the spread of COVID-19 has become a threat to global health.

Multiple studies have summarised the clinical manifestations and radiographic characteristics of COVID-19.[2-4] Compared with that in non-COVID-19 pneumonia patients, COVID-19 patients are

less likely to exhibit pleural effusions.[5] However, pleural effusion has been observed in severe and critical patients with COVID-19 as compared with that in moderate cases.[6,7] Moreover, pleural effusion is associated with a high rate of mortality and longer hospital stay for patients with community-acquired pneumonia.[8] Thus, whether pleural effusion indicates the poor prognosis of COVID-19 pneumonia remains to be investigated.

In this study, we analysed the differences between the clinical manifestations, laboratory examinations, imaging features and clinical outcomes among COVID-19 patients with or without pleural effusion.

2 | METHODS

2.1 | Sources of data

We retrospectively selected confirmed COVID-19 patients admitted to the Union Hospital, Tongji Medical College, Huazhong University of Science and Technology between the 20 January and 29 of February, 2020 for this study. Patients were confirmed based on the positive readout for SARS-CoV-2 nucleic acid in throat swabs using real-time polymerase chain reaction (RT-PCR).

We collected the medical records of the enrolled patients, including clinical features, laboratory results, imaging and clinical outcomes. The extent of pneumonia of patients were assessed using the CT scoring system as following: each of the five lung lobes was visually scored on a scale of 0-5:0 indicating no involvement; 1, <5% involvement; 2, >5%-25% involvement; 3, 26%-49% involvement; 4, 50%-75% involvement and 5, >75% involvement. The total score of all the five lobes was each patient's CT score (range from 5 to 25). After they were discharged, 217 of these patients returned to the outpatient department of the Union Hospital, Tongji Medical College, Huazhong University of Science and Technology. We also collected the computed tomography (CT) scans of the patients from their subsequent visits. Patients were followed up to 30 May 2020.

Ethics approval was obtained from the institutional ethics board of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (approval #2020-0120). Oral consent was obtained from all the patients. The need for written informed consent was exempt as per the ethics approval (2020-0120).

2.2 | Laboratory confirmation

Throat swabs were tested for the presence of SARS-CoV-2 using RT-PCR as per the recommendation by the World Health Organization.[9] The patient specimens from the upper respiratory tract were collected in tubes pre-filled with virus preservatives. Total RNA was extracted using the High Pure Viral RNA Kit (Roche, Basel, Switzerland). Two target genes were assayed to identify SARS-CoV-2 RNA, namely open reading frame1ab (ORF1ab) and nucleocapsid protein (N). Samples were considered positive (+) or negative (−) based on the "Novel Coronavirus Infected Pneumonia Lab Test Technical Guide Version 2," released by the National Health Commission & State Administration of Traditional Chinese Medicine on 22 January 2020.[10]

2.3 | Statistical analysis

Continuous variables have been represented as mean ± standard deviation or median and interquartile range (IQR). Categorical variables have been summarised as counts and percentages for each patient category. Statistical significance between groups was determined using unpaired t-test or chi-squared test as appropriate. All statistical analyses were performed using SPSS22.0 (SPSS Inc).

3 | RESULTS

3.1 | Clinical manifestations

In all, 827 patients with COVID-19 pneumonia were included in this study (Table 1). The mean age of the cohort was 51 years and 451 (54.53%) patients were males. We suspected contact exposure for 198 patients. At admission, 76 (9.19%) patients presented with pleural effusion based on their CT scans. Patients with pleural effusion were significantly older (60.72 ± 15.40 vs 49.96 ± 15.86 years $P < .001$), suffered dyspnoea more common (68.42% vs 27.16%, $P < .001$), and more likely to be severe (53.95% vs 32.05%, $P < .001$) or critical cases (27.63% vs 5.64%, $P < .001$) as compared with patients without pleural effusion. The number of days from the onset of symptoms to hospital admission was lower for patients with pleural effusion as compared with that for patients without pleural effusion (7 [IQR 3-10] vs 8 [IQR 5-12] days, $P < .002$).

3.2 | Laboratory and radiological findings

On admission, patients with pleural effusion had lower levels of white blood cells, lymphocytes, platelets, haemoglobin and Albumin as compared with those in patients without pleural effusion ($P < .05$, Table 2). Moreover, the levels of neutrophil, Aspartate aminotransferase, Lactic dehydrogenase, Creatine kinase, Prothrombin time, Activated partial thromboplastin time, D-Dimer and Erythrocyte sedimentation rate in patients with pleural effusion were much higher than those in patients without pleural effusion were ($P < .05$, Table 2). There was a higher proportion of patients with pleural effusion and higher levels of C-reaction protein or Procalcitonin as compared with those without pleural effusion ($P < .001$, Table 2). Table 3 shows that COVID-19 patients with pleural effusion showed a higher IL-6, IL-10 and TNF-α content and lower levels of CD8^{+} T cells ($P < .01$). According to CT image features, consolidation was more

TABLE 1 Characteristics and Symptoms of Patients with COVID-19 Pneumonia

	Total (n = 827)	Non-pleural effusion (n = 751)	Pleural effusion (n = 76)	P value
Age (mean, SD)	50.95 ± 16.11	49.96 ± 15.86	60.72 ± 15.40	<.001
Sex				
Male	451 (54.53)	411 (54.73)	40 (52.63)	.809
Female	376 (45.47)	340 (45.27)	36 (47.37)	
Suspected case contact exposure	198 (23.94)	183 (24.37)	15 (19.74)	.401
Current smoker	65 (7.86)	58 (7.72)	7 (9.21)	.646
Underlying illness				
Hypertension	182 (22.01)	159 (21.17)	23 (30.26)	.081
Coronary heart disease	28 (3.39)	26 (3.46)	2 (2.63)	>.999
Carcinoma	26 (3.14)	21 (2.80)	5 (6.58)	.081
Diabetes mellitus	98 (11.85)	84 (11.19)	14 (18.42)	.091
Chronic kidney disease	14 (1.69)	13 (1.73)	1 (1.32)	>.999
Respiratory disease	27 (3.26)	21 (2.80)	6 (7.89)	.031
Symptoms				
Fever (temperature ≥37.3℃)	647 (78.23)	591 (7.87)	56 (73.68)	.310
Cough	495 (59.85)	451 (60.05)	44 (57.89)	.714
Sputum	223 (26.96)	197 (26.23)	26 (34.21)	.138
Haemoptysis	15 (1.81)	14 (1.86)	1 (1.32)	.733
Chest pain	46 (5.56)	43 (5.73)	3 (3.95)	.792
Dyspnoea	256 (30.96)	204 (27.16)	52 (68.42)	<.001
Fatigue	372 (44.98)	339 (45.14)	33 (43.42)	.810
Myalgia	192 (23.22)	178 (23.70)	14 (18.42)	.392
Headache	122 (14.75)	114 (15.18)	8 (10.53)	.313
Diarrhoea	152 (18.38)	140 (18.64)	12 (15.79)	.642
Vomiting	44 (5.32)	39 (5.19)	5 (6.58)	.590
Disease severity status				
General	449 (54.29)	435 (57.92)	14 (18.42)	<.001
Severe	297 (35.91)	256 (34.09)	41 (53.95)	
Critical	81 (9.80)	60 (7.99)	21 (27.63)	
Days from symptom onset to hospital admission, median [IQR]	7 [5-12]	8 [5-12]	7 [3-10]	.002

Note: Values are expressed as n (%).

common in patients with pleural effusion as compared with that in patients without pleural effusion (47.37% vs 31.42%, *P* = .007; Table S1). Typical CT images are shown in Figure S1.

Among the 76 COVID-19 patients with pleural effusion, 62 patients were bilateral effusion, the rest 14 patients were unilateral pleural effusion. The amount of pleural effusion was small quantity in 73 patients, medium quantity in 3 patients. The CT scores of the patients with small quantity of pleural effusion had no

significant difference, to those with medium quantity of pleural effusion (12.84 ± 5.31 vs 16.67 ± 6.66, *P* = .23).

3.3 | Treatments and clinical outcomes

As shown in Table 4, all patients were administered antiviral agents, including Arbidol, Alpha-interferon, Ribavirin and Lopinavir/ritonavir.

TABLE 2 Laboratory findings of 827 patients infected with SARS-CoV-2 on admission to hospital

	Total (n = 827)	Non-pleural effusion (n = 751)	Pleural effusion (n = 76)	P value
White blood cell count, $\times 10^9$/L	5.40 ± 2.40	5.24 ± 2.15	6.10 ± 3.24	.002
<3.5, n (%)	162 (19.59)	147 (19.57)	15 (19.74)	.015
3.5–9.5, n (%)	617 (74.61)	566 (75.37)	51 (67.10)	
>9.5, n (%)	48 (5.80)	38 (5.06)	10 (13.16)	
Neutrophil count, $\times 10^9$/L	3.66 ± 2.30	3.43 ± 1.99	4.69 ± 3.14	<.001
Lymphocyte count, $\times 10^9$/L	1.22 ± 0.54	1.29 ± 0.54	0.93 ± 0.43	<.001
<1.1, n (%)	372 (44.98)	319 (42.47)	53 (69.74)	<.001
1.1–3.2, n (%)	453 (54.78)	430 (57.26)	23 (30.26)	
>3.2, n (%)	2 (0.24)	2 (0.27)	0 (0)	
Platelet count, $\times 10^9$/L	224.39 ± 94.80	229.53 ± 96.02	201.63 ± 86.15	.015
Haemoglobin, g/L	124.57 ± 15.54	125.91 ± 14.89	118.68 ± 17.07	<.001
ALB, g/L	36.92 ± 5.20	37.74 ± 4.87	33.30 ± 5.13	<.001
ALT, U/L	34.85 ± 32.38	34.57 ± 31.86	36.15 ± 34.85	.683
AST, U/L	33.63 ± 25.48	31.53 ± 21.63	42.93 ± 36.89	<.001
T-BIL, μmol/L	11.66 ± 5.78	11.45 ± 4.81	12.58 ± 8.89	.078
D-BIL, μmol/L	3.97 ± 2.46	3.98 ± 2.37	3.92 ± 2.86	.829
BUN, mmol/L	4.32 ± 2.19	4.27 ± 2.16	4.57 ± 2.30	.250
CREA, μmol/L	73.22 ± 29.81	72.6 ± 29.58	75.98 ± 30.84	.345
LDH, U/L	276.51 ± 129.03	262.98 ± 122.34	336.53 ± 141.71	<.001
CK, U/L	107.23 ± 165.92	100.01 ± 140.94	139.22 ± 246.79	.034
PT, s	13.44 ± 1.43	13.25 ± 1.11	14.29 ± 2.20	<.001
APTT, s	38.79 ± 4.47	38.39 ± 3.99	40.58 ± 5.87	<.001
D-Dimer, mg/L	1.373 ± 2.52	1.06 ± 1.84	2.77 ± 4.16	<.001
CRP, mg/L, n (%)				<.001
<8.0	292 (35.31)	283 (37.68)	9 (11.84)	
≥8.0	535 (64.69)	468 (62.32)	67 (88.16)	
PCT, μg/L, n (%)				<.001
<0.5	795 (96.13)	728 (96.94)	67 (88.16)	
≥0.5	32 (3.87)	23 (3.06)	9 (11.84)	
ESR, mm/h	37.68 ± 28.38	35.39 ± 27.66	47.83 ± 29.49	<.001

Abbreviations: ALB, Albumin; ALT, Alanine aminotransferase; APTT, Activated partial thromboplastin time; AST, Aspartate aminotransferase; BUN, Blood urea nitrogen; CK, Creatine kinase; CREA, Creatinine; CRP, C-reaction protein; D-BIL, Direct bilirubin; ESR, Erythrocyte sedimentation rate; LDH, Lactic dehydrogenase; PCT, Procalcitonin; PT, Prothrombin time; T-BIL, Total bilirubin.

Among these, 779 (94.20%), 126 (15.24%), 206 (24.91%) and 431 (52.12%) patients were co-administered antibiotics, corticosteroids, immunoglobulin and thymopeptide, respectively, during hospitalisation. There were no differences in drug therapy between these two groups. COVID-19 patients with pleural effusion were more likely to undergo high-flow nasal cannula oxygen therapy (13.16% vs 6.13%, P = .029), non-invasive mechanical ventilation (10.53% vs 2.93%, P = .004) and invasive mechanical ventilation (3.95% vs 0.67%, P = .030).

The incidence of respiratory failure and acute respiratory distress syndrome (ARDS) in patients with pleural effusion were significantly higher than that in patients without pleural effusion (44.74% vs 14.91% and 19.74% vs 6.26%, respectively; P < .001). Among the 827 patients, 28 died unfortunately. The rate of mortality in patients with pleural effusion was higher than that in patients without pleural effusion (7.89% vs 2.93%, P = .0361). The remaining 799 patients were discharged as of 17 April 2020. Among these discharged

TABLE 3 Cytokine and lymphocyte subsets in patients infected with SARS-CoV-2

	Total (n = 827)	Non-pleural effusion (n = 751)	Pleural effusion (n = 76)	P value
IL-2 (pg/mL; normal range 0.10-4.10)	2.73 ± 1.51	2.74 ± 1.67	2.67 ± 0.34	.730
IL-4 (pg/mL; normal range 0.10-3.20)	2.15 ± 1.39	2.17 ± 1.52	2.10 ± 0.56	.728
IL-6 (pg/mL; normal range 0.10-2.90)	26.52 ± 56.55	23.15 ± 59.34	41.45 ± 38.97	.009
Increased, n (%)	721 (87.18)	648 (86.29)	73 (96.05)	.011
IL-10 (pg/mL; normal range 0.10-5.00)	4.83 ± 4.17	4.52 ± 4.01	6.18 ± 4.53	<.001
Increased, n (%)	221 (26.72)	182 (24.23)	39 (51.32)	<.001
TNF-α (pg/mL; normal range 0.10-23.00)	4.09 ± 6.73	3.03 ± 3.17	8.48 ± 13.16	<.001
IFN-γ (pg/mL; normal range 0.10-18.00)	2.59 ± 3.55	2.61 ± 3.87	2.50 ± 1.46	.802
CD3$^+$ T cells (%; normal range 58.17-84.22)	72.13 ± 10.68	72.43 ± 10.67	70.8 ± 10.68	.205
CD4$^+$ T cells (%; normal range 24.34-51.37)	44.04 ± 9.96	43.74 ± 9.897	45.35 ± 10.2	.178
CD8$^+$ T cells (%; normal range 14.23-38.95)	24.13 ± 8.46	24.71 ± 8.67	21.55 ± 6.92	.002
B cells (%; normal range 4.10-18.31)	14.22 ± 6.55	13.99 ± 6.32	15.27 ± 7.42	.099
NK cells (%; normal range 3.33-30.47)	10.34 ± 6.99	10.26 ± 7.24	10.72 ± 5.79	.608
CD4$^+$/CD8$^+$ ratio (normal range 0.41-2.72)	2.12 ± 1.12	2.07 ± 1.14	2.36 ± 0.97	.036

Note: Values are expressed as Mean ± SD.

patients, the length of hospital stay and duration of viral shedding after the onset of COVID-19 was longer for patients with pleural effusion as compared with those for patients without pleural effusion (18 [IQR 13-26] vs 25 [IQR 18-31] days, P < .001; 24 [IQR 18-31] vs 26 [23-31], P < .05; respectively, Figure 1A,B). In all, 217 patients returned for follow-up CT scans at the Wuhan Union Hospital (41 and 176 patients with and without pleural effusion, respectively). CT scans showed that the mean duration for resolution of inflammation in the lung, after the onset of COVID-19, was longer in patients with pleural effusion as compared with that in patients without pleural effusion (49 [IQR 40-63] vs 66 [IQR 48-80] days, P < .001, Figure 1C).

3.4 | Risk factors associated with pleural effusion in COVID-19 patients

Using univariate analysis, we find several variables that showed significant difference between COVID-19 patients with pleural effusion and those without, including older age, had an underlying illness of respiratory disease (Table S2). All underlying illness and

other variables which showed statistical significance with P < .05 between two groups, were further processed using a multivariable logistic regression. As shown in Table S3, older age, history of respiratory disease, lower level of platelet and ALB, higher level of PT, APTT, D-Dimer and TNF-α were risk factors for pleural effusion in COVID-19 patients.

To evaluate the risk factors associated with pleural effusion further, patients with and without pleural effusion were matched in a 1:2 ratio (76:152 patients) based on age, gender and comorbidity (Table S4). Fourteen factors from the univariate analysis were used as part of the multivariate analysis to identify reliable prognostic factors for pleural effusion in patients with COVID-19 (Tables S5 and S6). Low platelet counts and high levels of TNF-α were risk factors for pleural effusion in COVID-19 (Table S6).
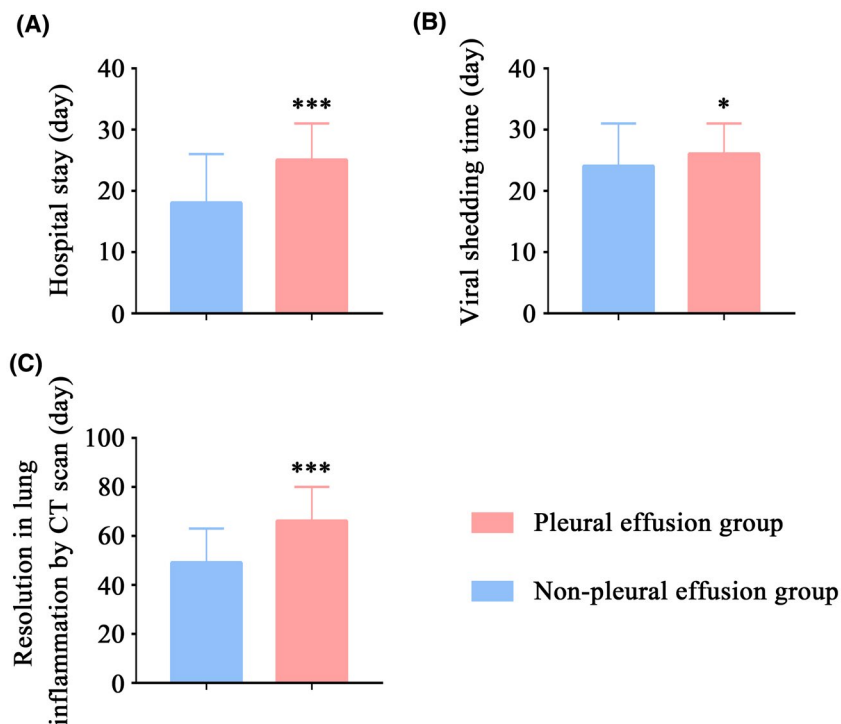
4 | DISCUSSION

In this retrospective cohort study, COVID-19 patients with radiologically defined pleural effusion at admission were older, more likely to

TABLE 4 Treatments and clinical outcomes of 827 patients with COVID-19

	Total (n = 827)	Non-pleural effusion (n = 751)	Pleural effusion (n = 76)	P value
Treatments				
Antibiotics	779 (94.20)	704 (93.74)	75 (98.68)	.116
Antiviral agent	827 (100)	751 (100)	76 (100)	>.999
Corticosteroids	126 (15.24)	109 (14.51)	17 (22.37)	.092
Immunoglobulin	206 (24.91)	182 (24.23)	24 (31.58)	.165
Thymopeptide	431 (52.12)	391 (52.06)	40 (52.63)	>.999
Oxygen inhalation through nasal catheter	402 (48.61)	363 (48.34)	39 (51.32)	.632
Mask oxygen inhalation	18 (2.18)	15 (2.00)	3 (3.92)	.225
High-flow nasal cannula oxygen therapy	56 (6.77)	46 (6.13)	10 (13.16)	.029
Non-invasive mechanical ventilation	30 (3.63)	22 (2.93)	8 (10.53)	.004
Invasive mechanical ventilation	8 (0.97)	5 (0.67)	3 (3.95)	.030
ECMO	6 (0.73)	5 (0.67)	1 (1.32)	.440
Clinical outcomes				
Respiratory failure	146 (17.65)	112 (14.91)	34 (44.74)	<.001
ARDS	62 (7.50)	47 (6.26)	15 (19.74)	<.001
Deceased	28 (3.39)	22 (2.93)	6 (7.89)	.0361

Note: Values are expressed as n (%).

Abbreviations: ARDS, Acute respiratory distress syndrome; ECMO, Extracorporeal Membrane Oxygenation.

FIGURE 1 (A) The length of hospital stays for COVID-19 patients. (B) The duration of viral shedding after the onset of COVID-19 in patients. (C) Time for resolution of lung inflammation as observed by computed tomography after the onset of COVID-19 in patients. Data have been represented as median and interquartile range. *$P < .05$, ***$P < .001$. Comparisons were made using the unpaired *t*-test

be severe or critical cases, exhibited a severe inflammatory response and more likely to suffer from respiratory failure or ARDS as compared with patients without pleural effusion. Furthermore, pleural effusion was associated with poor prognosis in COVID-19 patients, including higher mortality and longer duration of SARS-CoV-2 viral shedding and resolution of inflammation in the lungs.

Previous studies have shown pleural effusion in 5.3%-10.3% of COVID-19 patients.[6,7,11,12] In accordance with this, we observed pleural effusion in 9.19% of the COVID-19 patients. Patients with pleural effusion had similar symptoms (excluding dyspnoea) as those in patients without pleural effusion: dyspnoea was more common in COVID-19 patients with pleural effusion. Moreover, pleural effusion was associated with the severity of COVID-19: pleural effusion was observed in a larger percentage of severe or critical patients than that in moderate cases. Thus, pleural effusion may be an indicator of poor prognosis for SARS-CoV-2 infection.

Pleural effusion is associated with a higher 30-day rate of mortality and longer hospital stay for emergency patients with pneumonia.[8] Previous reports have also shown pleural effusion to indicate poor prognosis of adenovirus pneumonia, H5N1 viral pneumonia and acute Middle East respiratory syndrome coronavirus infection.[13-16] This study showed that COVID-19 patients with pleural effusion were associated with a greater rate of mortality, higher incidence of respiratory failure and ARDS, and longer hospital stay. This could be attributed to the exacerbated inflammatory response and progressing pneumonia.

Multiple laboratory tests showed differences between patients with and without pleural effusion. Patients with pleural effusion showed higher levels of white blood cells, neutrophils, CRP, PCT and ESR as compared with those in patients without pleural effusion. This indicated severe inflammation in patients with pleural effusion. Increased CRP and PCT are indicators of poor prognosis in COVID-19 patients.[17] Furthermore, patients with pleural effusion had higher levels of inflammatory cytokines, including IL-6, IL-10 and TNF-α, indicating an intense cytokine storm. As a pro-inflammatory mediator, excessive IL-6 results in a severe inflammatory response.[18] Tocilizumab, a humanised anti-IL-6 receptor antibody, has shown efficacy in COVID-19 patients.[19,20] IL-10 is a potent anti-inflammatory cytokine that induces T cell exhaustion and reduces inflammation.[21] During rhabdovirus infection, TNF-α inhibits the clearance of virus particles by hindering host antiviral response.[22] Inhibition of TNF-α signalling alleviates the pathogenic effects of SARS-CoV infection in mice.[23] Thus, there is an urgent need for clinical trials based on cytokine and anti-cytokine therapies for the treatment of COVID-19.[24]

Host immune cells play a pivotal role in infectious diseases. We observed low levels of lymphocytes and CD8^{+} T cells in COVID-19 patients with pleural effusion as compared with those in patients without pleural effusion. Moreover, the duration of SARS-CoV-2 particle shedding was longer among patients with pleural effusion. Previous studies have shown that increased IL-10 content and decreased CD8^{+} T cells are associated with prolonged duration of SARS-CoV-2 shedding.[25] Further studies are warranted to explore the underlying mechanism(s) involved in dysregulated immunity and SARS-CoV-2 infection.

Pleural effusion indicates severe pneumonia.[26] In this study, patients with pleural effusion were more likely to manifest with consolidation in CT scans at admission and required a longer time for the resolution of lung inflammation. The presence of consolidation indicated viral invasion into the respiratory epithelium, resulting in diffuse alveolar injury and inflammatory exudates.[7] Pleural effusion results from biological processes, such as increased interstitial oedema and capillary permeability.[27] In this study, multi-factor regression analysis showed that decreased platelet and increased TNF-α contents may be risk factors for pleural effusion. TNF-α is important for pleural inflammation and parapneumonic effusion.[28]

However, this study has several limitations. First, this was a single-centre retrospective study. Second, most patients with pleural effusion were not subjected to thoracentesis owing to the low level of pleural effusion, thereby limiting the potential for understanding the aetiology of pleural effusion. Third, only some of the discharged patients returned for a follow-up examination. This prevented the study of resolution of lung inflammation in all the patients. Thus, multi-centre retrospective studies are needed to understand the clinical outcome of COVID-19 patients with pleural effusion in the future.

5 | CONCLUSIONS

In summary, COVID-19 patients with pleural effusion had higher rates of mortality, respiratory failure and ARDS, and experienced longer hospital stay. Thus, pleural effusion may serve as an indicator of poor prognosis among COVID-19 patients.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethics approval was obtained from the institutional ethics board of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (approval #2020-0120). Oral consent was obtained from all the patients. The need for written informed consent was exempt as per the ethics approval (2020-0120).

CONFLICT OF INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

QZ and JCZ conceived the idea, designed and supervised the study, had full access to all data and took responsibility for the integrity of the data. XSW and XW, collected and analysed the clinical and laboratory data. LLY, YRN, WBP and ZHW evaluated pulmonary computed tomographic images. XSW analysed data and performed statistical analysis. All authors reviewed and approved the final version.

DATA AVAILABILITY STATEMENT

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

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the Supporting Information section.