Kidney involvement in covid 19 virus

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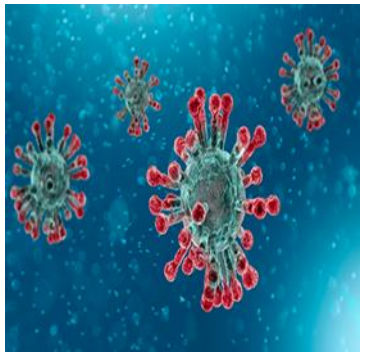

coronavirus disease 19

- In December 2019, an acute respiratory infectious disease caused by a novel coronavirus occurred in Wuhan, Hubei Province, China, which is now officially named as **“coronavirus disease 19 (COVID-19)”** by the WHO
- The disease has spread rapidly from Wuhan to other regions in China.

- Whether the patients with coronavirus disease 19 (COVID-19) infected by severe acute respiratory syndrome (SARS)-CoV-2 would commonly develop acute kidney injury (AKI) is an important issue worthy of clinical attention

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Coronavirus Disease 19 Infection Does Not Result in Acute Kidney Injury: An Analysis of 116 Hospitalized Patients from Wuhan, China

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- In this study, 116 COVID-19-confirmed patients were enrolled, who were hospitalized in the Department of Infectious
- All COVID-19 patients enrolled in this study were laboratory confirmed
- cases, which were identified with nucleic acid detection of SARS-CoV-2 from a throat swab samples using reverse transcription-polymerase chain reaction (RT-PCR).

- The recorded information includes demographic data, medical history, contact history, potential comorbidities, symptoms, signs, laboratory test results, chest computer tomography (CT) scans and treatment measures (i.e., antiviral therapy, glucocorticoid usage, breathing support, kidney replacement therapy).

Standard Definitions of Acute Kidney Injury

- AKI in adults is one of the following: an increase in serum creatinine (SCr) by ≥26 μmol/L (0.3 mg/dL) within 48 h, or an increase in SCr to > 1.5 times baseline within the previous 7 days, or urine volume < 0.5 mL/kg/h for > 6 h.

Chronic Kidney Disease Diagnosis

- The standard definition of chronic kidney disease (CKD) is glomerular filtration rate of < 60 mL/min/1.73 m_2, or markers of kidney damage (such as albuminuria, urine sediment abnormalities, electrolyte, and other abnormalities due to tubular disorders, Abnormalities detected by histology, Structural abnormalities detected by imaging, history of kidney transplantation), or both, of at least 3 months duration, regardless of the underlying cause

Table 1. Baseline characteristics of 116 COVID-19-confirmed patients

	Total (n = 116)	Clinical categories of pneumonia			p value
		mild (n = 59)	severe (n = 46)	ARDS (n = 11)	
Age, years, median (IQR)	54 (38–69)	45 (27–56)	52 (35–64)	67 (58–81)	<0.001
Gender, n (%)					
Male	67 (57.8)	34 (57.6)	27 (58.7)	6 (52.0)	1.000
Female	49 (42.2)	25 (42.4)	19 (41.3)	5 (45.5)	1.000
Comorbidities, n (%)					
Hypertension	43 (37.1)	23 (38.9)	15 (32.6)	5 (45.5)	0.533
Diabetes	18 (15.5)	8 (13.6)	6 (13.0)	4 (36.4)	0.067
Malignant tumors	12 (10.3)	1 (1.7)	5 (10.9)	6 (52.0)	<0.001
Cerebral infarction	7 (6.0)	1 (1.7)	4 (8.7)	2 (18.2)	0.132
CKD	5 (4.3)	0	5 (10.9)	0	1.000

p values indicate differences between ARDS and non-ARDS patients. $p < 0.05$ was considered statistically significant.

CKD, chronic kidney disease; IQR, interquartile range; COVID-19, coronavirus disease 19; ARDS, acute respiratory distress syndrome.

Table 2. Changes of kidney function in 116 COVID-19-confirmed patients

COVID-19-confirmed patients (n = 116)	Number	BUN, mmol/L 3.6–9.5	SCr, μmol/L 57–111	eGFR, mL/min >90
Without CKD				
1st week	111	5.23±1.72	78.26±25.14	129.81±10.33
2st week	108	5.58±2.44	75.31±23.52	126.37±9.72
3st week	105	5.04±1.96	77.04±22.27	128.53±9.29
4st week	104	5.19±2.07	72.95±24.83	127.96±9.65
p value		0.877	0.121	0.177
With CKD				
1st week	5	32.08±8.58	937.61±114.62	14.43±7.34
2st week	5	30.66±9.64	955.47±141.09	15.96±8.72
3st week	5	29.79±10.37	897.53±175.48	21.33±10.09
4st week	5	31.94±9.18	914.29±163.87	22.86±9.37
p value		0.981	0.801	0.152

p values indicate differences between 4st week and 1st week. $p < 0.05$ was considered statistically significant.

BUN, blood urea nitrogen; SCr, serum creatinine; eGFR, glomerular filtration rate; COVID-19, coronavirus disease 19; CKD, chronic kidney disease.

Result:

- At present, none of the patients exhibited acute renal failure.
- In addition, the patients with CKD were still undergoing regular continuous renal replacement therapy (CRRT) except for the treatment of COVID-19.
- In the course of treatment, the monitoring

of renal function indicators showed stable state, without exacerbation of CKD, and reexamination of CT showed that pulmonary inflammation was gradually absorbed.

Detection Data of SARS-CoV-2 RNA in Urine Sediment

- SARS-CoV-2 RNA in urine sediments of COVID- 19-confirmed 53 patients, including 5 CKD cases, enrolled in this study was examined by real-time RT-PCR.
- The results showed that SARS-CoV-2 RNA in urine sediments

was positive in 3 patients without CKD (3/48),

- There was no significant difference in the characteristics and clinical course between those with and without positive SARS-CoV-2 RNA in urine sediments

- It is worth noting that all of 5 patients with CKD were survived, who did not develop to ARDS or CKD deterioration.

- It was also suggested that CRRT plays an important role in the treatment of COVID-19 complicated with CKD.
- In the event of signs of AKI, potential interventions, including CRRT, should be used to protect renal function as early as possible.
- AKI was uncommon in COVID-19. SARS-CoV-2 infection does not result in AKI, or aggravate CKD in the COVID-19 patients.

EDTA-ERA

- ***Kidney involvement seems to be frequent in patients with Covid-19. Proteinuria (and/or blood in urine) often occurs at the beginning or during the infection, a few patients even develop acute kidney injury (AKI). This shows that Covid-19 also attacks the kidneys.***

- ***Given the involvement of kidneys during coronavirus infection, patients should also be monitored after the disease***

Acute renal impairment in coronavirus-associated severe acute respiratory syndrome

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• We conducted a retrospective analysis of the plasma creatinine concentration and other clinical parameters of the 536 SARS patients with normal plasma creatinine at first clinical presentation, admitted to two regional hospitals following a major outbreak in Hong Kong in March 2003.

Kidney tissues from seven other patients with postmortem examinations were studied by light microscopy and electron microscopy.

• Among these 536 patients with SARS, 36 (6.7%) developed acute renal impairment occurring at a median duration of 20 days (range 5–48 days) after the onset of viral infection despite a normal plasma creatinine level at first clinical presentation.

- The acute renal impairment reflected the different prerenal and renal factors that exerted renal insult occurring in the context of multiorgan failure

- Eventually, 33 SARS patients (91.7%) with acute renal impairment died.
- The mortality rate was significantly higher among patients with SARS and acute renal impairment compared with those with SARS and no renal impairment (91.7% vs. 8.8%) ($P < 0.0001$).

- **Renal tissues revealed predominantly acute tubular necrosis with no evidence of glomerular pathology.**

Conclusion

- Acute renal impairment is uncommon in SARS but carries a high mortality.
- The acute renal impairment is likely to be related to multi-organ failure rather than the kidney tropism of the virus.
- The development of acute renal impairment is an important negative prognostic indicator for survival with SARS.

Table 1. Various laboratory and clinical parameters of patients with acute renal impairment and normal kidney function

Variable	Renal impairment ($N = 36$)	Normal renal function ($N = 500$)	P value
Age *years*	53.5 (34–77)	38.0 (18–96)	<0.001
Systolic blood pressure *mm Hg*	130.5 (105–200)	125.0 (96–210)	0.013
Diastolic blood pressure *mm Hg*	70.0 (54–100)	70.0 (40–109)	0.942
Hemoglobin g/dL[a]	14.0 (8.4–16.9)	13.2 (7.6–18)	0.035
White blood cells ($\times 10^9$/L)[a]	6.5 (1.8–16.3)	5.30 (1.55–27.3)	0.005
Neutrophil ($\times 10^9$/L)[a]	5.00 (0.8–15.5)	3.90 (0.7–26.3)	0.004
Lymphocyte ($\times 10^9$/L)[a]	0.80 (0.3–2.8)	0.80 (0.2–3.1)	0.556
Platelet ($\times 10^9$/L)[a]	151.0 (79–285)	163.0 (41–893)	0.671
Prothrombin time *second*[a]	11.9 (10.2–14.1)	12.0 (0.4–120)	0.391
Activated partial thromboplastin time *second*[a]	33.2 (23.3–87)	32.2 (14–120)	0.092
Plasma sodium *mmol/L*[a]	132.0 (126–140)	134.0 (121–144)	0.001
Plasma potassium *mmol/L*[a]	3.7 (2.8–6.1)	3.6 (2.2–8.1)	0.634
Plasma urea *mmol/L*[a]	4.6 (1.8–16)	3.4 (0.3–18.6)	<0.001
Plasma creatinine *μmol/L*[a]	93.5 (48–128)	70.0 (40–123)	<0.001
Plasma albumin *g/L*[a]	34.0 (23–44)	38.0 (20–50)	<0.001
Plasma alanine aminotranferase *U/L*[a]	49.0 (12–193)	26.0 (3–587)	0.001
Plasma lactate dehydrogenase *U/L*[a]	311.0 (148–990)	218.5 (30–1669)	<0.001
Nadir hemoglobin *g/dL*	8.7 (3.4–15.5)	11.3 (3.9–15.8)	<0.001
Nadir white blood cells ($\times 10^9$/L)	5.35 (1.8–10.5)	4.00 (0.8–20.5)	0.003
Nadir lymphocyte ($\times 10^9$/L)	0.30 (0.1–0.7)	0.40 (0–7.3)	<0.001
Plasma peak creatine phosphokinase *U/L*	222.0 (26–22974)	96.0 (11–7154)	<0.001
Symptomatic days before admission	1.0 (1–3)	3.0 (1–15)	0.071

[a]Measurement at first admission.

Table 2. Risk factors of mortality in severe acute respiratory syndrome (SARS) by univariate analysis

	Relative risk (99% CI)	*P* value
Use of inotropes	15.77 (7.539–32.99)	<0.001
Acute renal impairment	16.91 (8.368–34.16)	<0.001
Acute respiratory distress syndrome	10.28 (4.854–21.77)	<0.001
Systolic blood pressure	1.014 (0.997–1.031)	0.032
White blood cells	1.066 (0.988–1.150)	0.029
Lymphocyte count	0.529 (0.209–1.339)	0.077
Nadir white blood cells	1.160 (1.057–1.272)	<0.001
Nadir lymphocyte count	0.016 (0.001–0.217)	<0.001
Plasma albumin on admission	0.890 (0.841–0.942)	<0.001
Peak plasma creatine phosphokinase > 1500[a]	6.689 (1.699–26.34)	<0.001
Plasma alanine aminotransferase on admission	1.005 (1.001–1.009)	0.004
Age	1.049 (1.029–1.068)	<0.001

[a]Patients with creatine phosphokinase less than 1500 serve as the reference group.

Table 3. Independent risk factor predicting mortality in severe acute respiratory syndrome (SARS) by multivariate analysis

	Adjusted relative risk (99% CI)	*P* value
Acute renal impairment	4.057 (1.461–11.27)	<0.001
Acute respiratory distress syndrome	3.286 (1.141–9.463)	0.004
Age	1.033 (1.008–1.058)	0.001
Plasma albumin on admission	0.936 (0.876–0.999)	0.009

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editorial

The Novel Coronavirus 2019 epidemic and kidneys

OPEN

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KEYWORDS: acute kidney injury; hemodialysis

■ ■ ovel Coronavirus disease (COVID-19) is ...amination of the chest (bilateral lobular and

Pathogenesis of kidney injury

- The exact mechanism of kidney involvement is unclear:

postulated mechanisms include sepsis leading to cytokine storm syndrome or direct cellular injury due to the virus.

Angiotensin converting enzyme and dipeptidyl peptidase-4, both expressed on renal tubular cells, were identified as binding partners for SARS-CoV

and MERS-CoV, respectively

- Viral RNA has been identified in kidney tissue and urine.

Recently, Zhong's lab in Guangzhou successfully isolated SARS-CoV-2 from the urine sample of an infected patient, suggesting the kidney as the target of this novel coronavirus.

Treatment

- The current treatment of COVID-19 with AKI includes general and supportive management and kidney replacement therapy.

- There is no effective antiviral therapy available at present.

Treatment

- Continuous renal replacement therapy (CRRT) has been successfully applied in the treatment of SARS, MERS, and sepsis.[22,23] High-volume hemofiltration in a dose of 6 l/h removed inflammatory cytokines (IL-6) and improved the Sequential Organ Failure Assessment scores at day 7 in patients with sepsis.[2]
- Therefore, CRRT may play a role in patients with COVID-19 and sepsis syndrome.

The potential role of extracorporeal therapy techniques needs to be evaluated

COVID-19 in patients with kidney disease

- Pregnant women, newborns, the elderly, and patients with comorbidities like diabetes mellitus, hypertension, and cardiovascular disease are susceptible to COVID-19 infection and are likely to have more severe illness often requiring care from an intensive care unit.
- The impact of COVID-19 on chronic kidney disease

has not been reported.[30]

- COVID-19 infection presents a special threat to patients on dialysis. There are 7184 patients on hemodialysis (HD) in 61 treatment

centers in Wuhan City.

- At a single HD center in Renmin Hospital, Wuhan University, 37 out of

230 patients on HD and 4 of 33 staff members developed COVID-19 infection between January 14 and February 17, 2020.

30 A total of 7 patients on HD died, of whom 6 had COVID- 19 infection.

- However, the deaths were deemed to be due to cardiovascular causes and not directly to the COVID-19 infection.
- Patients on HD with COVID-19 had less lymphopenia, lower serum levels of inflammatory cytokines, and milder clinical disease than other patients with COVID-19 infection.

Management of patients on dialysis

- COVID-19 infection presents particular challenges for patients on dialysis, in particular, those in in-center HD.
- Patients with uremia are particularly vulnerable to infection and may exhibit greater variations in clinical symptoms and infectivity.
- In-center HD significantly increases the risk of transmission of infection, including to medical staff and facility workers, patients themselves, family members, and all others.

Kidney involvement in COVID-19 infection

- In previous reports of SARS and MERS-CoV infections, acute kidney injury (AKI) developed in 5% to 15% cases and carried a high (60%–90%) mortality rate.

- Early reports suggested a lower incidence (3%–9%) of AKI in those with COVID-19 infection

proteinuria

- A study of 59 patients with COVID-19 found that 34% of patients developed massive albuminuria on the first day of admission, and 63% developed proteinuria during their stay in hospital

- Blood urea nitrogen was elevated in 27% overall and in two-thirds of patients who died.

- Computed tomography scan of the kidneys showed reduced density, suggestive of inflammation and edema

- Cheng et al.[13] recently reported that amongst 710 consecutive hospitalized patients with COVID-19, 44% had proteinuria and hematuria and 26.7% had hematuria on admission

- The prevalence of elevated serum creatinine and blood urea nitrogen was 15.5% and 14.1%, respectively.

- AKI was an independent risk factor for patients’ in-hospital mortality

Treatment

- General management
- Antiviral therapy.
- Extracorporeal treatments
- Glucocorticoids
- Convalescent plasma
- Monoclonal antibody

Management of patients on dialysis

- The Chinese Society of Nephrology[31] and the Taiwan Society of Nephrology[32] have recently developed guidelines for dialysis units during the COVID-19 outbreak

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editorial: special report

Kidney disease is associated with in-hospital death of patients with COVID-19

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In December 2019, a coronavirus 2019 (COVID-19) disease outbreak occurred in Wuhan, Hubei Province, China, and rapidly spread to other areas worldwide. Although diffuse alveolar damage and acute respiratory failure were the main features, the involvement of

Table 1 | Characteristics and outcomes of patients with COVID-2019

Variables	All patients	Normal baseline serum creatinine	Elevated baseline serum creatinine	*P* value
Number	701	600	101	
Age, yr	63 (50–71)	61 (49–69)	73 (62–79)	<0.001
Male patients	367 of 701 (52.4)	294 of 600 (49.0)	73 of 101 (72.3)	<0.001
Days from illness onset to admission, d	10 (7–13)	10 (7–13)	9 (7–12)	0.381
Fever on admission	213 of 655 (32.5)	187 of 560 (33.4)	26 of 95 (27.4)	0.246
Systolic blood pressure, mm Hg	128 (117–143)	128 (118–142)	128 (114–144)	0.942
Diastolic blood pressure, mm Hg	79 (72–87)	79 (73–87)	77 (70–86)	0.282
Severe disease	297 of 701 (42.4)	244 of 600 (40.7)	53 of 101 (52.5)	0.026
Any comorbidity	297 of 698 (42.6)	237 of 598 (39.6)	60 of 100 (60.0)	<0.001
Chronic kidney disease	14 of 698 (2.0)	5 of 598 (0.8)	9 of 100 (9.0)	<0.001
Chronic obstructive pulmonary disease	13 of 698 (1.9)	9 of 598 (1.5)	4 of 100 (4.0)	0.191
Hypertension	233 of 698 (33.4)	185 of 598 (30.9)	48 of 100 (48.0)	0.001
Diabetes	100 of 698 (14.3)	84 of 598 (14.0)	16 of 100 (16.0)	0.606
Tumor	32 of 698 (4.6)	28 of 598 (4.7)	4 of 100 (4.0)	0.965
Admission to intensive care unit	73 of 701 (10.4)	60 of 600 (10.0)	13 of 101 (12.8)	0.382
Administration of mechanical ventilation	97 of 701 (13.4)	75 of 600 (12.5)	22 of 101 (21.8)	0.012
Acute kidney injury	36 of 701 (5.1)	24 of 600 (4.0)	12 of 101 (11.9)	0.001
Stage 1	13 of 701 (1.9)	10 of 600 (1.7)	3 of 101 (3.0)	0.356
Stage 2	9 of 701 (1.3)	4 of 600 (0.7)	5 of 101 (5.0)	
Stage 3	14 of 701 (2)	10 of 600 (1.7)	4 of 101 (4.0)	
In-hospital death	113 of 701 (16.1)	79 of 600 (13.2)	34 of 101 (33.7)	<0.001

COVID-19, coronavirus disease 2019.

Data are presented as number/total (percentage) or median (interquartile range). The severity was staged based on the guidelines for diagnosis and treatment of COVID-19 (trial fifth edition) published by the Chinese National Health Commission on February 4, 2020.

Incidence of AKI and in-hospital death.

- During hospitalization, AKI occurred in 5.1% of patients.
- The incidence of AKI was significantly higher in patients with elevated baseline serum creatinine (11.9%) than in patients with normal baseline values (4.0%)

- In-hospital death occurred in 16.1% of patients.
- The median time to death was 6 days (interquartile range, 3–12 days).
- The incidence of in-hospital death in the patients with

elevated baseline serum creatinine was 33.7%, which was significantly higher than in those with normal baseline serum creatinine (13.2%)

Association of kidney disease indicators with in-hospital death.

- Kaplan-Meier analysis revealed a significantly higher in-hospital death rate for patients with kidney abnormalities, including elevated baseline serum creatinine, elevated baseline BUN, proteinuria, hematuria, and AKI ($P < 0.001$)

Risk factors for in-hospital death

- the following were all associated with in-hospital death:

  proteinuria of any degree,

  hematuria of any degree,

  elevated baseline BUN,

  serum creatinine, peak serum creatinine > 133 mmol/l,

  and AKI over stage 2

- The etiology of kidney disease involvement in patients with COVID-19 is likely to be multifactorial

1-First, the novel coronavirus may exert direct cytopathic effects on kidney tissue

- This is supported by the detection of polymerase chain reaction fragments of corocoronavirus in blood and urine in both the patients with the 2003 SARS virus[18] and those with COVID-19

2-the novel coronavirus uses angiotensin converting enzyme 2 (ACE2) as a cell entry receptor, which is identical to that of the SARSCoV as reported in 2003.

3-deposition of immune complexes of viral antigen or virus-induced specific immunological effector mechanisms (specific T-cell lymphocyte or antibody) may damage the kidney.

4-virus-induced cytokines or mediators might exert indirect effects on renal tissue, such as hypoxia, shock, and rhabdomyolysis.

5-drugs

Potential biochemical markers to identify severe cases among COVID-19 patients

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Potential biochemical markers to identify severe cases among COVID-19 patients

There is a high mortality and long hospitalization period for severe cases with 2019 novel coronavirus disease (COVID-19) pneumonia. Therefore, it makes sense to search for a potential biomarker that could rapidly and effectively identify severe cases early

- Clinical samples from 28 cases of COVID-19 (8 severe cases, 20 mild cases) in Zunyi District from January 29, 2020 to February 21, 2020 were collected and otherwise statistically analysed for biochemical markers

- Serum urea, creatinine (CREA) and cystatin C (CysC) concentrations in severe COVID-19 patients were significantly higher than those in mild COVID-19 patients ($P<0.001$), and there were also significant differences in serum direct bilirubin (DBIL), cholinesterase (CHE) and lactate dehydrogenase (LDH) concentrations between severe and mild COVID-19 patients ($P<0.05$).
- Serum urea, CREA, CysC, DBIL, CHE and LDH could be used to distinguish severe COVID-19 cases from mild COVID-19 cases.

- In particular, serum biomarkers, including urea, CREA, CysC, which reflect glomerular filtration function, may have some significance as potential indicators for the early diagnosis of severe COVID-19 and to distinguish it from mild COVID-19.
- Glomerular filtration function injury in severe COVID-19 patients should also be considered by clinicians.

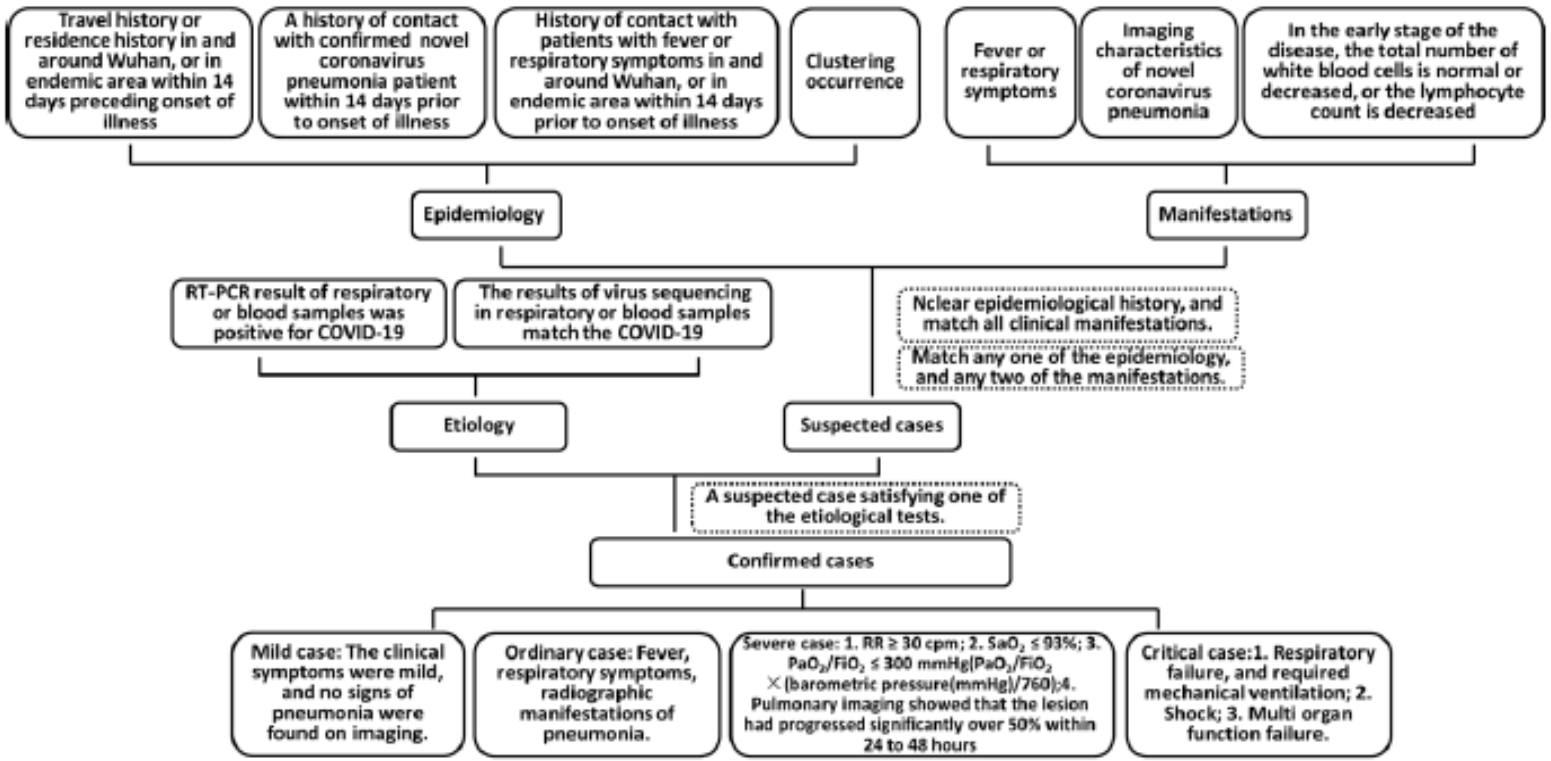
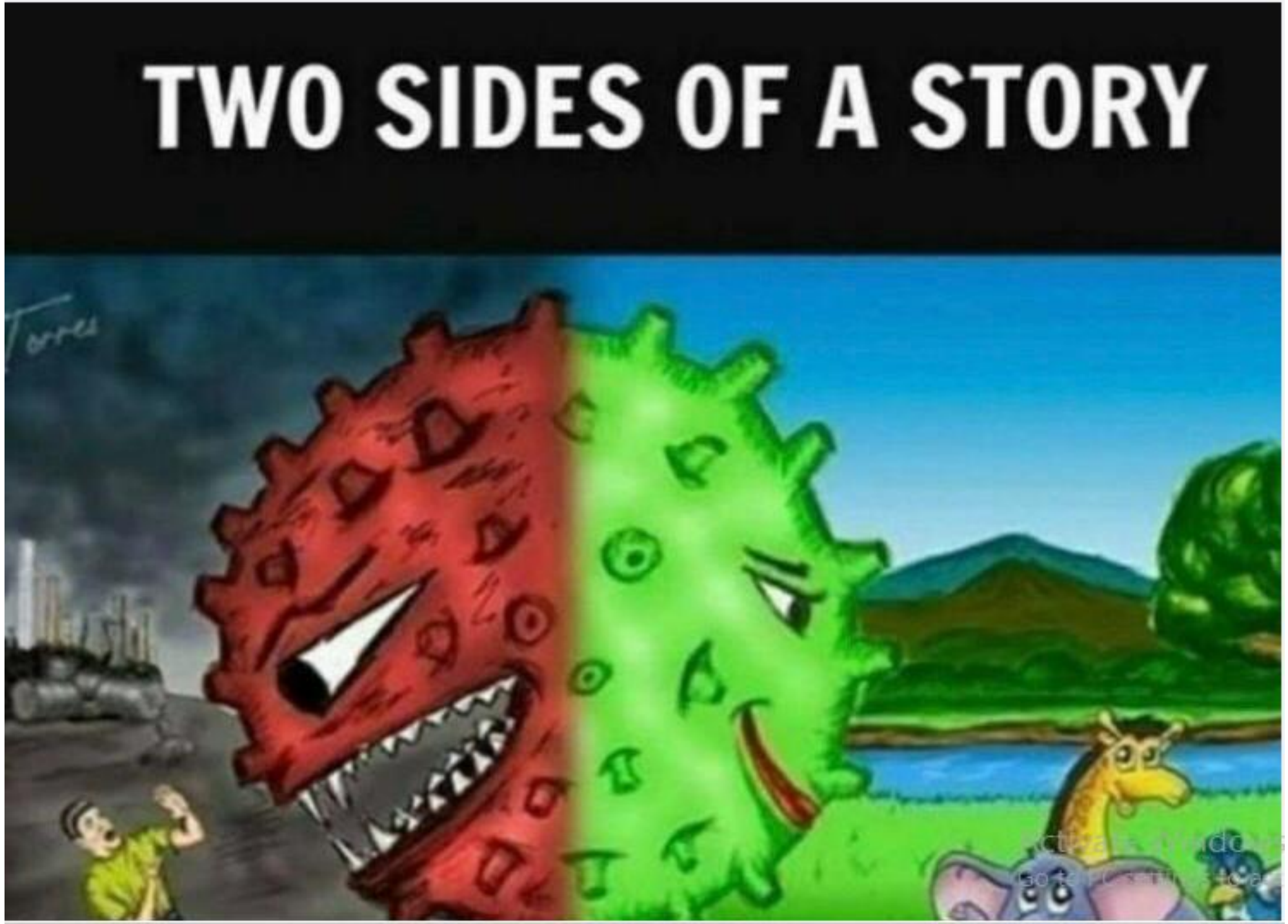


Figure 1. Chart representing the guidelines for the diagnosis of novel coronavirus pneumonia.

The analysis included 4,166 test results from 28 COVID-19 patients, including 8 confirmed


TWO SIDES OF A STORY