Relationship Between serum SARS-CoV-2 nucleic acid (RNAemia) and Organ Damage in COVID-19 Patients: A Cohort Study

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Summary

Among 85 COVID-19 patients, 32 had RNAemia and of these 18 had organ damage and 10 died during hospitalization. RNAemia was significantly associated with organ damage and in-hospital mortality.
Abstract

**Background:** SARS-CoV-2 has spread worldwide and has the ability to damage multiple organs. However, information on serum SARS-CoV-2 nucleic acid (RNAemia) in patients affected by COVID-19 is limited.

**Methods:** Patients who admitted to Zhongnan Hospital of Wuhan University with laboratory-confirmed COVID-19, were tested SARS-CoV-2 RNA in serum from January 28, 2020, to February 9, 2020. Demographic data, laboratory findings, radiological, comorbidities and outcomes data were collected and analyzed.

**Results:** 85 patients were included in the analysis. The viral load of throat swabs was significantly higher than serum samples. The highest detection of SARS-CoV-2 RNA in serum samples was between 11 to 15 days after the symptom onset. Analysis to compare with and without RNAemia provided evidence that CT and some laboratory biomarkers (total protein, BUN, LDH, hypersensitive troponin I and D-dimer) were abnormal, and that the extent of these abnormalities was generally higher in RNAemia than in non-RNAemia. Organ damages (respiratory failure, cardiac damage, renal damage and coagulopathy) were more common in RNAemia than non-RNAemia. Patients with vs without RNAemia had shorter durations from serum testing SARS-CoV-2 RNA. The mortality rate was higher among patients with vs without RNAemia.

**Conclusions:** This study provides evidence to support that SARS-CoV-2 may have an important role in multiple organ damage, such as respiratory failure, cardiac damage, renal damage and coagulopathy. We did not find strong evidence that SARS-CoV-2 plays a role in damage of liver and the central nervous system. And our evidence suggests that RNAemia has a significant association with a higher risk of in-hospital mortality.

**Keywords:** RNAemia; SARS-CoV-2; COVID-19; organ damage
**Introduction**

As of March 30, 2020, coronavirus disease 2019 (COVID-19) were 707416 confirmed cases worldwide, including 33272 deaths (4.7% fatality rate). Understanding clinical aspects of the pathogenesis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may serve to better define targets for developing new therapeutic, preventive, and disease-monitoring strategies. Based on recently published work, SARS-CoV-2 exists not only in the lower respiratory tract, but also in blood [1-3]. However, the rate of detection of SARS-CoV-2 RNA in blood by different researchers is different. Wang et al found that the viremia was present in only 3 out the 307 patients studied [4]. In contrast, Zheng et al reported to find that 35 out of 96 patients had, in fact, a detectable viral load in serum samples [5]. Meanwhile, marked biochemical abnormalities, reflecting the potential capability of the virus to produce damage in different body compartments, have been observed [6-11]. Nevertheless, studies exploring the relationship between RNAemia, biochemical abnormalities, and clinical disorders are scanty. Using a retrospective approach, we conducted an analysis to explore the potential association between the RNAemia and lung damage, cardiac damage, liver damage, renal impairment, and coagulation abnormalities.

**Methods**

**Study design and patients**

Consecutive patients who admitted to Zhongnan Hospital of Wuhan University with confirmed COVID-19, were tested SARS-COV-2 RNA in serum from January 28, 2020 to February 9, 2020, which included in this retrospective cohort study. The COVID-19 patients enrolled in this study were diagnosed according to World Health Organization interim guidance. The cases with incomplete original reports were excluded.

This study was reviewed and approved by the Medical Ethics Committee of Zhongnan Hospital of Wuhan University (approval number 2020037).
**Data collection**

Clinical characteristics, laboratory findings, radiological features, and outcomes were collected from electronic medical records. Confirmed organ damage complications were based on the discharge diagnosis in electronic medical records. Laboratory assessments consisted of a complete blood count, C-reactive protein, procalcitonin, coagulation test, liver and renal function and cardiac markers. All information was obtained through standardized data collection forms. Two researchers independently reviewed the data collection forms to ensure data quality.

**Sample collection and SARS-CoV-2 RNA extraction**

All of the throat swabs and serum samples were collected from COVID-19 patients for extracting SARS-CoV-2 RNA. After collection, the throat swabs were placed into a collection tube containing 200μL of virus preservation solution, and total RNA was extracted within 3 hours using the respiratory sample RNA isolation kit (Zhongzhi, Wuhan, China). Briefly, 40μL of cell lysates were added into a collection tube followed by vortex for 10 seconds. After standing at room temperature for 10 minutes, the collection tube was centrifugated at 1000rpm/min for 5 minutes. The suspension was used for real-time reverse transcriptase–polymerase chain reaction (RT-PCR) assay of SARS-CoV-2 RNA.

Peripheral blood (2mL) was collected from patients with COVID-19 into red-cap tubes. Then serum were separated using centrifugation at 1500rpm for 5 min. After separation, all serum samples were immediately stored at -80°C for total RNA extraction. Total RNA extraction from 200μL of serum sample was performed using a commercial nucleic acid isolation kit (Daan Gene, Guangzhou, China) according to manufacturer’s instruction, the extracted RNA was stored at -80°C for further study.

**Real-time RT-PCR assay of SARS-CoV-2 RNA**

SARS-CoV-2 RNA was amplified using a real-time RT-PCR assay kits (Daan Gene, Guangzhou, China), which was carried out in an Eppendorf tube with an ABI prism 7500 (Thermo Fisher Scientific, Waltham, MA, USA). Two target genes, including open reading frame 1ab (ORF1ab) and nucleocapsid protein(N), were simultaneously amplified and tested during the real-time RT-PCR assay. Target 1 (ORF1ab): forward primer CCCTGTGGGTTTTACACTTAA; reverse primer ACGATTGTGCATCAGCTGA; and the probe 5’-VIC-CCGCTCTGCGGTATGTGGAAAGGTTATGG-BHQ1-3’. Target 2 (N): forward primer
GGGAATTCTCTCTGCTAGAAT; reverse primer CAGACATTTTGCTCTCAAGCTG; and the probe 5′-FAM- TTGCTGCTGCTTGACAGATT-TAMRA-3′. The final amount of the real-time RT-PCR reaction mixture was 25μL, including 17μL of NC(ORF1ab/N) solution A, 3μL of NC(ORF1ab/N) solution B, and 5μL of SARS-CoV-2 RNA solution. Real-time RT-PCR assay was performed under the following conditions: incubation at 50 °C for 15 minutes and 95 °C for 15 minutes, 45 cycles of denaturation at 94 °C for 15 seconds, and extending and collecting fluorescence signal at 55 °C for 45 seconds. Monitoring of fluorescence was carried out at regular intervals during the extension phase. The cycle threshold (Ct) values obtained from the multiple real-time RT-PCR assays were adopted to identify whether SARS-CoV-2 RNA was present in tested sample. The detection limit of quantitative PCR reaction was 500 copies/mL. According to the manufacturer’s procedures, a Ct value of less than 40 was defined as a positive result, and a Ct value of 40 or more was defined as a negative result. Viral load was calculated by plotting Ct values onto the standard curve constructed based on the standard product.

Chest CT images were analyzed using an Artificial Intelligence (AI) system provided by Shanghai United Imaging Intelligence Healthcare. The software segmented and then calculated the infected regions, including the whole, left and right lung, 5 lung lobes, 18 sections and their corresponding infected area. The calculated parameters involved the volume, percentage of these areas and the volume, distribution at four different HU ranges ([-, -750), [-750, -300), [-300, 49), [50, +]) in infected area. Two senior radiologists with intermediate and senior titles independently participated in the image processing task to check if the segmentation of the lesions was accurate.

Definitions

Fever was defined as temperature of at least 37.3°C. Septic shock was defined according to the 2016 Third International Consensus Definition for Sepsis and Septic Shock[2]. Respiratory failure was defined as arterial blood oxygen partial pressure (PaO₂) <60 mmHg, with or without carbon dioxide partial pressure (PaCO₂) >50 mmHg at sea level, resting state, and breathing air conditions, excluding intracardiac anatomical shunt and primary cardiac output factors such as reduction. Cardiac injury
was diagnosed if serum levels of cardiac biomarkers (e.g., highsensitive cardiac troponin I) were above the 99th percentile upper reference limit, or if new abnormalities were shown in electrocardiography and echocardiography[2]. Renal injury was diagnosed according to the KDIGO clinical practice guidelines[12]. Hepatic injury was defined to alanine aminotransferase(ALT) or aspartate aminotransferase(AST) ≥3 × upper limit of normal (ULN) or total bilirubin ≥ 2 × ULN, regardless of whether there is previous liver disease[13]. Coagulopathy was defined as a 3-second extension of prothrombin time or a 5-second extension of activated partial thromboplastin time. The illness severity of COVID-19 was defined according to the Chinese management guideline for COVID-19 (version 7.0)[14]. Mild cases include non-pneumonia or mild pneumonia. Severe disease refers to dyspnoea, respiratory rate ≥30/ min, blood oxygen saturation ≤93%, partial pressure of arterial oxygen to fraction of inspired oxygen ratio <300, or lung infiltrates >50% within 24 to 48 hours.

Statistical analysis

Statistical analysis was performed using SPSS 23.0 (IBM Corp., Armonk, New York, USA). Continuous and categorical variables were presented as median (interquartile range, IQR) and n (%), respectively. The Student’s t-test was used to compare continuous variables, which conform to a normal distribution, while the Chi-square test was used to compare categorical variables between the two groups. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using multiple logistic regression. Survival curves were plotted using the Kaplan-Meier method and compared between patients with vs without RNAemia using the log-rank test. Statistical significance was defined with p<0.05.

Results

151 COVID-19 patients were tested SARS-COV-2 RNA in serum at Zhongnan Hospital of Wuhan University from January 28, 2020, to February 9, 2020. There were 184 serum samples in 151 patients. 47 of 184 serum samples were positive and 137 were negative through real-time RT-PCR. However, the core data sets (including clinical outcomes and symptoms) of 66 patients were lacking due to incomplete original reports, this report delineates 85 inpatients in the final analysis, with
categorizing 32 and 53 patients into positive and negative subgroups, respectively. There were 118 serum samples and 356 throat swabs of 85 patients. Among them, 14 of 32 positive patients and 13 of 53 negative patients have done more than two throat swabs or serum tests of SARS-CoV-2 RNA (Figure 1). The total positive rate in the serum samples and throat swabs was 28.81% and 54.49%, respectively. The viral load of throat swabs was significantly higher than serum samples (P< 0.0001). The median duration of virus in serum samples (11 days, IQR 8-14 days) was similar with in throat swabs (12 days, IQR 7-17 days; P=0.489). The highest detection of SARS-CoV-2 RNA in serum samples was between 11 to 15 days after the symptom onset (Figure 2 and Supplementary Table 1).

The demographic and clinical characteristics are shown in Supplementary Table 2. The median age of the 85 patients was 56.0 years, and 43 were females. 49.41% patients had a history of exposure to SARS-CoV-2. Hypertension was the most common comorbidity, followed by cardiovascular disease and diabetes. The distributions of comorbidities were no statistical difference for the positive and negative groups. The most common symptoms on admission were cough and myalgia or arthralgia or fatigue, followed by shortness of breath and fever. During hospital admission, the highest respiratory rate and cough were significantly more common in positive cases as compared with negative cases (P < .050). Further studies, the meaningful variables selected by the chi-square test were evaluated using multiple logistic regression analysis. Significant factors were found on highest temperature during hospital admission <37.5°C (OR = 0.086, P < .050), and cough (OR = 0.330, P < .050) (Supplementary Table 3).

Figure 3A shows a flowchart for laboratory and CT scan data collection. Since not all 118 serum samples had laboratory data within the time frame we specified, 85 patients took the first positive or negative time in serum. In 85 laboratory data, 71.76% patients had lymphopenia. Most patients demonstrated reduced albumin to globulin ratio and albumin, and elevated levels of C-reactive protein. Positive cases had more prominent laboratory abnormalities (eg, neutrophilia, reduced total protein, elevated blood urea nitrogen, increased lactate dehydrogenase, increased hypersensitive troponin I and D-dimer levels) as compared with negative cases (P < .050) (Table 1 and Supplementary Table 4).
CT images were selected 3 days before and after the detection of RNAemia, and 2 patients did not meet the criteria. Four patients had only X-rays due to serious illness, so 79 patients underwent chest CT scans. In total, 50 parameters were obtained from each set of CT images, including the volume and percentage of lung infection areas and each of its substructures. Table 1 showed that lung infected proportion in the positive cases was more severe compared with the negative cases, which had a significant difference in the left upper superior lingular and right lower anterior basal lobes (P < .050). Furthermore, by setting different HU ranges, it was found that HU [-300,49] and HU [50+) in the positive cases had more infection volumes (P < .050). More laboratory tests and CT image analysis are shown in Supplementary Table 4 and Table 5.

During hospital admission, organ damages (P < .001) were more common in patients with RNAemia than those without RNAemia and included respiratory failure (P < .001), followed by cardiac damage (P < .050), renal damage (P < .050) and coagulopathy (P < .050). This result was consistent with previous laboratory tests. Patients with RNAemia vs those without RNAemia had shorter durations from serum testing SARS-CoV-2 RNA (P < .050). The severe symptoms (P < .050) and mortality rate (P < .050) were higher among patients vs without RNAemia as shown in the Table 2 and Kaplan-Meier survival curves in Figure 3C. In-depth study of RNAemia patients, the mean viral loads in serum samples was lower in severe than in mild, but the difference was not significant (Figure 3D).

Discussion

In this study, we shed light on the association between the level of SARS-CoV-2 RNAemia and organ damage using data from real clinical practice. There are several important findings from our study.

First, we compared positive samples between the throat and serum. The viral load of throat swabs was significantly higher than serum samples, which was consistent with current study [5]. It was further found that the positive percentage of serum samples was higher than throat swabs around days 0-15 after the symptom onset, it seems that PCR carried out on serum is more sensible than PCR.
carried out on respiratory sample, it needs to be confirmed with a larger samples. And the peak of SARS-CoV-2 RNA in serum was around days 11-15 after the symptom onset, however the peak of SARS-CoV in plasma was around day 3 after the symptom onset[16], maybe this is reason why the condition of SARS patients deteriorates faster than SARS-CoV-2. SARS-CoV caused 8096 confirmed cases and 774 deaths (9.6% fatality rate) in 29 countries from November 2002 to July 2003[15]. As of March 30, 2020, the fatality rate of COVID-19 was 4.7%. The fatality rate of SARS-CoV-2 is currently lower than SARS-CoV. 

Second, in the current study, the risk of RNAemia among highest temperature during hospital admission >39.0 °C was 11.63-times higher than <37.5 °C. Patients with cough were 3.03-times more likely to catch RNAemia than those without cough. This was consistent with previous studies, which patients with SARS-CoV-2 were more easier to catch fever and cough[17]. Among 85 COVID-19 patients, 23 patients had organ damage, 18 of which were RNAemia. One of the most serious complications was respiratory failure. By setting different HU ranges, it was found that HU [-300,49) and HU [50+) were more infected in RNAemia patients, which represented the lung consolidation and blood vessels, respectively. This is consistent with autopsy analysis revealing pulmonary vascular congestion and inflammatory clusters with fibrinoid material and multinucleated giant cells[18]. The next severely damaged organ was the heart. Myocardial enzyme biomarkers in our study indicated cardiac damage due to increased lactate dehydrogenase and hypersensitive troponin I in RNAemia patients, which was supported by the fact that the median values of cardiac abnormality markers were higher in patients with heart injury than those without in a cohort of 416 patients diagnosed with COVID-19[6, 7]. The third combined organ kidney was damaged with reduced total protein and elevated blood urea nitrogen in RNAemia patients. Those findings are consistent with the previous articles[19]. In addition, RNAemia patients demonstrated high coagulopathy with elevated D-dimer levels in our study. D-dimer greater than 1µg/L is associated with fatal outcome of COVID-19, although its underlying mechanism is unclear[11]. It is speculated that the induction of procoagulant factors and hemodynamic changes predispose to ischemia and thrombosis[20].
Multiple organ damage with RNAemia mentioned above may be related to the binding of the SARS-CoV-2 S protein to the membrane receptor angiotensin converting enzyme II (ACE2) on the host cell. ACE2 receptor has been documented to express in alveoli, heart, and kidneys[21], and was approximately 10- to 20-fold higher affinity for SARS-CoV-2 than SARS-CoV, since the “down” conformation of SARS-CoV-2 was angled closer to its center[22]. In addition, the SARS-CoV-2 S glycoprotein harbors a furin cleavage site at the boundary between the S1/S2 subunits, which helps expand the spread of the virus, and coupled with the transport of blood, it is more conducive to the virus reaching the organs and causing damage[23]. Also, some scholars propose that the extensive replication of coronavirus in the alveoli results in the breakdown of the alveolar vessel, and then the virus leaks into the bloodstream, allowing the virus to spread throughout the body[24].

Third, viral encephalitis or viral meningitis can occur in RNAemia, but no clinical manifestations of central nervous system invasion have been found in our study. However, SARS-CoV-2 was found in cerebrospinal fluid of a patient with COVID-19 in China, and loss of taste or smell of patients were confirmed COVID-19 in Japan and Korea. It warns medical staff of the dangers of the central nervous system infected by SARS-CoV-2 and to improve its detection in cerebrospinal fluid.

Finally, the current study documents that RNAemia patients had severe symptoms and high mortality rates, suggesting that SARS-CoV-2 RNAemia levels are strongly associated with unfavorable clinical outcome. 12 of the 32 RNAemia patients were mild patients in our study, which was inconsistent to the previous studies. The two teams found that all positive in blood (6 of 57) or in serum (5 of 48) were severe, respectively[3, 24]. However, SARS-CoV-2 RNA was found in serum of mild patients in our study, the mean Ct value of severe patients was lower than that of mild patients, which means that the viral load in severe patients is relatively large, although there is no statistically significant difference. This may also be due to a “positive” PCR result reflecting only the detection of viral RNA and does not mean or indicate presence of viable virus[25]. This requires further observation of viral activity by cell culture in vitro later. RNAemia Patients presented increased neutrophils and C-reactive protein as well as decreased lymphocytes in our study. It indicated inflammatory response caused by viral invasion, which might induce cytokine storms or
hyperinflammation leading to high mortality rates[26]. Chen et al. suggested that the extremely high interleukin 6 (IL-6) level was closely correlated with the incidence of RNAemia and mortality[3], which increased the credibility of our conclusion.

Our study has some limitations. First, under the premise of controlled transmission in Wuhan, the present study lacks evidence from magnetic resonance imaging to determine the features of the kidney, heart and other organs for gaining better insight. Second, further follow-up is needed to study whether long-term organ damage will occur in patients with negative SARS-CoV-2 in blood after hospital discharge.

In conclusion, our study provides new evidence to support the hypothesis that SARS-CoV-2 may play an important role in multiple organ damage, such as respiratory failure, cardiac damage, renal damage and coagulopathy. We did not find strong evidence that SARS-CoV-2 plays a role in damage of liver and the central nervous system. RNAemia has a significant association with organ damage of COVID-19 patients, and it is associated with a higher risk of in-hospital mortality. Although the underlying mechanism of RNAemia needs to be further explored, the findings presented here highlight the need to perform routine examination of blood virus in the clinic, which can potentially detect RNAemia early, guide clinicians to targeted treatment in order to prevent multiple organ damage.
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HBX had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis, including and especially any adverse effects. DX, FLZ and WBS contributed equally. DX and WBS made substantial contributions to the study concept and design. DX was in charge of the manuscript draft. LL and HL collected clinical data and confirmed data accuracy. WBS and FX collected CT images and confirmed data accuracy. FLZ and VBK participated in drafting the manuscript, and revising it on the basis of reviewers’ comments. DX and WBS made substantial contributions to data acquisition and analysis. YL made contributions to interpretation. LJC and YRL was in charge of the laboratory tasks, including sample processing and detection. HBX and XHW made substantial revisions to the manuscript.

Conflict of interest

All No reported conflicts of interest.
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Figure 1.

A, Flowchart of patient recruitment. B, Results of SARS-CoV-2 RNA detection in serum samples. C, Date distribution of positive and negative samples in 118 serum samples of 85 patients from January 28, 2020, to February 9, 2020. D, Date distribution of positive and negative samples in 356 throat swabs of 85 patients during hospitalization.

Figure 2.

A, Comparison of SARS-CoV-2 RNA viral load by sample types. Colored bars represent means and black bars represent standard deviation. B, Duration of detection of SARS-CoV-2 RNA by sample types. Colored bars represent medians and black bars represent interquartile ranges. C, Compared the detection of SARS-CoV-2 RNA in throat and serum samples. The rate of detection of SARS-CoV-2 RNA was highest in the throat and serum samples detected between 6 to 15 days and 11 to 15 days after the symptom onset, respectively.

Figure 3.

A, Flowchart for laboratory and CT scan data collection. Laboratory data were selected 1 days before and after collecting the serum samples of patients. CT images were selected 3 days before and after collecting the serum samples of patients. B, Distribution of disease severity and results of SARS-CoV-2 RNA detection in 85 patients. C, Kaplan-Meier survival curves for mortality during the time from serum sampling for SARS-CoV-2 RNA. D, Comparison of SARS-CoV-2 RNA viral load by disease severity in 32 RNAemia patients. Colored bars represent means and black bars represent standard deviation.
Table 1. Laboratory findings and AI system in the chest CT of patients with COVID-19 during hospitalization

| Laboratory findings                                   | Total (n=85)       | Positive (n=32) | Negative (n=53) | P Value |
|--------------------------------------------------------|--------------------|-----------------|-----------------|---------|
| Neutrophil count ≥ 6.3 × 10^9/L - No. , %              | 27/85(31.76)       | 17/32(53.13)    | 10/53(18.87)    | 0.001   |
| C-reactive protein level ≥ 10 mg/liter - No. , %       | 40/60(66.67)       | 12/17(70.59)    | 28/43(65.12)    | 0.685   |
| Procalcitonin level ≥ 0.05 ng/ml - No. , %             | 32/80(40.00)       | 16/28(57.14)    | 16/52(30.77)    | 0.022   |
| Total protein ≤ 65 g/L - No. , %                       | 23/85(27.06)       | 21/32(65.63)    | 22/53(41.51)    | 0.031   |
| Blood urea nitrogen ≥ 7.6 μmol/L - No. , %             | 24/85(28.24)       | 14/32(43.75)    | 10/53(18.87)    | 0.014   |
| Creatine kinase ≥ 171 U/L - No. , %                    | 12/58(20.69)       | 8/23(34.78)     | 4/35(11.43)     | 0.069   |
| Creatine kinase-MB ≥ 25 U/L - No. , %                  | 12/70(17.14)       | 7/29(24.14)     | 5/41(12.20)     | 0.192   |
| Lactate dehydrogenase ≥ 243 U/L - No. , %              | 24/60(40.00)       | 14/25(56.00)    | 10/35(28.57)    | 0.033   |
| Hypersensitive troponin I ≥ 26.2 pg/mL - No. , %       | 11/40(27.5)        | 9/19(47.37)     | 2/21(9.52)      | 0.020   |
| D-dimer ≥ 500 mg/L - No. , %                           | 32/75(42.67)       | 16/27(59.26)    | 16/48(33.33)    | 0.029   |

AI system in the chest CT

| Lesion distribution - median (IQR) | Total(n=79) | Positive(n=29) | Negative(n=50) | P Value |
|-----------------------------------|-------------|----------------|----------------|---------|
| Left upper lobe proportion (%)    |             |                |                |         |
| Apicoposterior                    | 0.8(0-6.9)  | 0.4(0-7.85)    | 0.85(0-6.2)    | 0.349   |
| Anterior                          | 0.3(0-5.3)  | 1.5(0-8.15)    | 0.3(0-4.125)   | 0.398   |
| Superior lingular                 | 1.6(0-8.5)  | 2.9(0-42.3)    | 1.55(0-4.475)  | 0.039   |
| Inferior lingular                 | 0.8(0-5.0)  | 1.6(0-1-25.05) | 0.6(0-3.7)     | 0.063   |
| Right lower lobe proportion (%)   |             |                |                |         |
| Dorsal                            | 5.9(0.1-36.8)| 11.8(0-77.65)  | 3.85(0.1-28.0) | 0.059   |
| Medial basal                      | 0.4(0-6.9)  | 2.8(0-15.85)   | 0.05(0-3.35)   | 0.077   |
| Anterior basal                    | 1.8(0-21.5) | 2.6(0-05-52.15)| 0.95(0-14.85)  | 0.035   |
| Lateral basal                     | 8.7(0.2-43.1)| 18.7(3.1-59.2) | 7.4(0.175-30.725) | 0.157   |
| Posterior basal                   | 7.3(0-24.8) | 10.5(0.45-38.1)| 5.0(0-20.825)  | 0.149   |

consolidation
Laboratory data were selected 1 days before and after collecting the serum samples of patients. CT images were selected 3 days before and after collecting the serum samples of patients. The Student’s t-test was used to compare median (interquartile range, IQR) between the two groups. the Chi-square test was used to compare n (%) variables between the two groups.

|                      | HU[ - 300, 49) volume (cm³) | HU[ - 300, 49) proportion (%) | vascular |
|----------------------|-----------------------------|-------------------------------|----------|
|                      | 35.4(4.5-110.8)             | 76.9(14.6-181.55)             |          |
|                      | 26.3(3.075-82.975)          | 0.038                         |          |
|                      | 0.9(0.1-3.4)                | 1.9(0.3-5.8)                  | 0.6(0.1-2.8) | 0.071   |
|                      | 0.038                       | 0.071                         |          |
| HU[ 50 + ) volume (cm³) | 6.3(0.6-27.9)              | 18.7(3.65-41.15)             | 5.1(0.5-20.425) | 0.029   |
| HU[ 50 + ) proportion (%) | 0.2(0-0.8)                 | 0.5(0.1-1.5)                 | 0.1(0-0.625)   | 0.065   |


Table 2. Complications and clinical outcomes of 85 patients with COVID-19.

| Complications – No. , % | Total(n=85) | Positive(n=32) | Negative(n=53) | P Value |
|-------------------------|-------------|----------------|----------------|---------|
| Septic shock            | 5/85(5.88)  | 3/32(9.38)     | 2/53(3.77)     | 0.557   |
| Organ injury            | 23/85(27.06)| 18/32(56.25)   | 5/53(9.43)     | 0.000   |
| Respiratory failure     | 18/85(21.18)| 15/32(46.88)   | 3/53(5.66)     | 0.000   |
| Cardiac injury          | 13/85(15.29)| 9/32(28.13)    | 4/53(7.55)     | 0.025   |
| Renal injury            | 9/85(10.59) | 7/32(21.88)    | 2/53(3.77)     | 0.024   |
| Hepatic injury          | 1/85(1.18)  | 1/32(3.13)     | 0              | 0.798   |
| Coagulopathy            | 5/85(5.88)  | 5/32(15.63)    | 0              | 0.013   |
| Multi-organ injuries(organ ≥ 2) | 18/85(21.18) | 13/32(40.63)   | 5/53(9.43)     | 0.001   |
| Clinical outcomes - No. , % |
| Severe                  | 41/85(48.24)| 20/32(62.50)   | 21/53(39.62)   | 0.041   |
| Discharge from hospital | 69/85(81.18)| 19/32(59.38)   | 50/53(94.34)   | 0.000   |
| Death                   | 13/85(15.29)| 10/32(31.25)   | 3/53(5.66)     | 0.004   |
| Staying in hospital     | 4/85(4.71)  | 3/32(9.38)     | 1/53(1.89)     | 0.293   |

The Student’s t-test was used to compare median (interquartile range, IQR) between the two groups. the Chi-square test was used to compare n (%) variables between the two groups.
Figure 1

**A** 151 patients in medical record system
- 45 with RNAemia (29.80%)
- 106 without RNAemia (70.20%)
- 66 patients excluded incomplete original reports

**B** 184 serum samples for detecting SARS-CoV-2 RNA in 151 patients
- 47 positive for nucleic acid (25.54%)
- 137 negative for nucleic acid (74.46%)
- 66 patients excluded incomplete original reports

**C**

- X-axis: Date of detecting SARS-CoV-2 RNA in serum
- Y-axis: Number of samples

**D**

- X-axis: Date of detecting SARS-CoV-2 RNA in serum
- Y-axis: Number of samples
- Diagram showing data distribution over time.
Figure 3

A. Time axis showing day of testing SARS-CoV-2 RNA in serum.

B. Flow diagram showing the distribution of patients:
- 32 patients (57.65%) serum positive
- 55 patients (62.35%) serum negative
- 20 patients (62.5%) severe
- 22 patients (37.5%) mild
- 21 patients (39.62%) severe
- 32 patients (60.38%) mild

C. Cumulative survival with and without RNAemia.

D. Cycle threshold in serum showing mild and severe groups with P=0.133.