



Research Article

Assessment of the Effects of SARS-Cov-2 Infection on Multiple Organs Using Laboratory Indices

Jianwei Zhou^{1*}, Yu Li², Cui Kong³, Yizhao Li⁴, Yao Liang⁵

1- Medical Laboratory, Hospital of Jining Medical University, Jining City, Shandong Province, China

2- Medical College, Jining Medical University, Jining City, Shandong Province, China

3- Nursing Department, Hospital of Jining Medical University, Jining City, Shandong Province, China

4- Rehabilitation Department, Fangan Rehabilitation Hospital of Jinan City, Jinan, China

5- Health School of Jining City, Jining City, Shandong Province, China

* Corresponding author: immunolife@126.com

ABSTRACT

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Keywords: SARS-Cov-2, COVID-19, laboratory result, liver, heart, kidney



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Background: Severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) is still a severe threat for human health currently, and the researches about it is a focus topic worldwide.

Aim of the study: In this study, we will collect some laboratory results of the patients with coronavirus disease (COVID-19) to assess the function of liver, heart, kidney and even pancreas.

Subjects and Methods: Laboratory results of the patients with COVID-19 are collected. The biochemical indices are classified and used to assess the according function of liver, heart, kidney; meantime, and blood glucose is also observed and taken as an index to roughly evaluate pancreas.

Results: There were some indices exhibited abnormal. For patient 1, the ratio of albumin and globulin slightly was lower than the down-limit of reference range. For patient 2, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT), creatine kinase (CK), creatinine kinase-MB isoenzyme (CK-MB), lactate dehydrogenase (LDH), alpha-hydroxybutyric dehydrogenase (HBDH), and beta-2 microglobulin (β 2-MG) were respectively higher than the according upper limit of the reference range, while prealbumin (PA) was lower than the down limit. For patient 3, GGT, CK, PA were high than normal range. For patient 4, CK, LDH, HBDH were higher than the upper range.

Conclusion: Infection of SARS-Cov-2 could cause liver and heart injury, and it is suggested that clinicians and researchers should pay more attention on the prevention, treatment and causative mechanism of such an injury.

Introduction

In early December 2019, several cases with pneumonia of unknown aetiology has been reported in Wuhan, Hubei, China, and rapidly attracted great attention nationally and worldwide.(1-3) Subsequently, the causative pathogen was isolated from the patients

with is first isolated from three patients with coronavirus disease 2019 (COVID-19) and officially named severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2).(4,5) So far, SARS-Cov-2 has spread hundreds of countries outside China and made more than

one million of persons infected and nearly one hundred thousand of death.(6)

Clinical and pathological features of patients with COVID-19 have recently been reported, which showing that SARS-Cov-2 infection causes clusters of severe and even fatal pneumonia.(3,7) The common symptoms of this pneumonia includes fever, fatigue, and dry cough, followed always by anorexia, myalgia, dyspnea, and so on.(2,8) Presently, except for lung injury caused by SARS-Cov-2, some researchers found that the new coronavirus also affected other multiple organs, especially including the three most important ones: hear,(9) kidney(10) and liver(11). Generally, these findings are not extracted from surgery or autopsy but laboratory tests.

In this study, we collected the laboratory results of the patients with COVID-19 which confirmed with quantitative reverse transcription polymerase chain reaction using the primers and probes targeting the ORF1ab and N genes of SARS-Cov-2. Through analyzing the changes of the biochemical indices, we assess if there are effects on the multiple organs in the patients under the condition of SARS-Cov-2 infection.

Subjects and Methods

Four patients who infected with SARS-Cov-2 were enrolled from the infectious disease department of Affiliated Hospital of Jining Medical University, Shandong Province, China. The patients' information and relative data were collected from the electric medical recorders and laboratory information system. These case series were approved by the Ethic Commission of Affiliated Hospital.

In order to further observe trends of the possible changes, the laboratory results of 20 health persons were also collected from the examination department of our hospital and used to make comparison with those of the patients infected with SARS-Cov-2.

All the patients and the healthy were excluded from the infection of other causative pathogens, such as hepatitis B and C virus, influenza A virus, parainfluenza virus, human immunodeficiency virus, mycoplasma pneumoniae, Chlamydia pneumoniae, and so on. Besides, there was no evidence for everyone related to tumor, hepatitis, cardiovascular disease, renal lesions and recent systemic antiviral therapy

Basic materials

Zhao J, female, 40-year old; Chen T, male, 34-year old; Jia YL, female, 60-year old; Wang HD, male, 58-year old. They were described as P1, P2, P3 and P4 in the study, respectively.

Biochemical indices

A relatively complete laboratory tests had been carried out for each of the patients, and 28 biochemical indices of the tests were extracted from tests, which including : alanine aminotransferase (ALT), aspartate aminotransferase (AST), total protein (TP), albumin (ALB), globulin (GLO), ratio of ALB versus GLO (A/G), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), gamma-glutamyltransferase (GGT), alkaline phosphatase (ALP), creatine kinase (CK), creatinine kinase-MB isoenzyme (CK-MB), lactate dehydrogenase (LDH), alpha-hydroxybutyric dehydrogenase (HBDH), Creatine (Cr), blood urea (BUR), uric acid

(UA), glucose (GLU), potassium (K⁺),sodium (Na⁺), chloridion (Cl), supercarbonate (HCO₃⁻), prealbumin (PA), beta-2 microglobulin (β₂-MG), ratio of AST versus ALT (AST/ALT), superoxide dismutase (SOD), cystatin C (CysC).

Statistical analysis

The data were reorganized with Microsoft Excel (WPS office system) and analyzed using SPSS 19.0 software. P value less than 0.05 was considered that there was a statistical difference between the matching data.

Results

The laboratory results for the four patients

There were some indices exhibited normal. For P1, only A/G was slightly less than the lower limit of reference range; For P2, ALT, AST, GGT, CK, LDH, HBDH, β₂-MG were higher than the upper limit while PA lower out of normal range; For P3, GGT, CK, PA were out of the range ; For P4, CK, LDH, HBDH and AST/ALT were exceed the upper range while ALB, A/G and PA were lower than the down-limit (as shown in Table 1).

In all the indices, the outrange ratios of CK and PA were the highest (75%). A/G, GGT, LDH and HBDH followed with the similar ratio of 50%. There was one patient exhibited out of the reference range for ALT, AST, ALB, β₂-MG and AST/ALT and the outrange ratio were all 25%. All the remianders, including TP, GLO, TBIL, DBIL, IBIL, ALP, CK-MB, CERA, BUR, UA, GLU, K⁺, Na⁺, Cl⁻, HCO₃⁻, SOD and CysC, were normal (Table 1)

Table1: Laboratory results of four patients with SARS-CoV-2 infection

Indices	P1	P2	P3	P4	Ref. range	Outrange ratio
ALT, U/L	21.8	148.9▲	24.4	19.1	7-40	25%
AST, U/L	25	127▲	31	32	13-35	25%
AST/ALT	1.15	0.85	1.27	1.68▲	0.8-1.5	25%
TP, g/L	69.2	67.2	68.4	65.3	65-85	0%
ALB, g/L	40.0	42.6	42.0	38.1▼	40-55	25%
GLO, g/L	29.2	24.6	26.4	37.2	20-40	0%
A/G	1.4▼	1.7	1.6	1.4▼	1.5-2.5	50%
TBIL, μmol/L	10.3	12.5	13.6	11.2	3.4-21	0%
DBIL, μmol/L	3.8	4.8	3.0	5.2	0-8	0%
IBIL, μmol/L	6.5	7.7	10.6	6.0	0-16.1	0%
GGT, U/L	29	81▲	48▲	37	7-45	50%
ALP, U/L	69	66	79	55	40-240	0%
CK, U/L	50	920▲	212▲	253▲	5-200	75%
CK-MB, ng/L	0.38	2.54	1.73	0.43	0-5	0%
LDH, U/L	183	364▲	223	364▲	90-240	50%
HBDH, U/L	126	266▲	178	256▲	80-220	50%
Cr, μmol/L	47.6	75.7	59.5	63.5	25-123	0%

BUR, mmol/L	2.50	3.50	3.00	4.00	2.29-7.2	0%
UA, μmol/L	202	270	247	236	142-339	0%
GLU, mmol/L	5.1	4.5	5.4	6.0	3.9-6.1	0%
K ⁺ , mmol/L	3.95	3.98	3.86	3.97	3.5-5.3	0%
Na ⁺ , mmol/L	139	138	145	143	137-147	0%
CL ⁻ , mmol/L	102	101	107	105	96-108	0%
HCO ₃ ⁻ , mmol/L	21.9	23.1	26.2	26.2	22-29	0%
PA, mg/L	218	152▼	147▼	133▼	200-400	75%
β ₂ -MG, mg/L	2.99	3.38▲	2.66	2.65	0-3	25%
SOD, U/ml	166	170	191	134	110-215	0%
CysC, mg/L	0.68	1.18	0.84	0.70	0.55-1.25	0%

▲ means more than the upper limit of the reference range; ▼ means more than the lower limit of the reference range; Ref. is the abbreviation of reference.

Table2: Comparison of laboratory results between four patients with SARS-Cov-2 infection and healthy persons

Indices	Mean (patient)	Mean (health)
ALT, U/L	53.6 [#]	17.4
AST, U/L	53.8 [#]	18.4
AST/ALT	1.2	1.1
TP, g/L	37.5 [#]	74.8
ALB, g/L	40.7	48.3
GLO, g/L	29.4	26.5
A/G	1.5	1.9
TBIL, μmol/L	11.9	15.5
DBIL, μmol/L	4.2	4.1
IBIL, μmol/L	7.7	11.4
GGT, U/L	48.8 [#]	17.5
CK, U/L	358.8 [#]	101.9
CK-MB, ng/L	1.3 [#]	7.8
LDH, U/L	283.5 [#]	167
HBDH, U/L	206.5 [#]	132.6
Cr, μmol/L	61.6	81.5
BUR, mmol/L	3.3	4.7
UA, μmol/L	238.8	304
GLU, mmol/L	5.3	4.9

means there is significant difference for the laboratory result between the two populations.

Comparison between the patients and healthy persons

The average age of the four patients with SARS-Cov-2 infection was 48 years old (ranged from 36 to 60), and that for the healthy persons were 45 years old (ranged from 27 to 62). There was no significant difference between the two groups (P>0.05).

As shown in Table 2, the mean values of some biochemical indices were calculated and compared between the patients with SARS-Cov-2 infection and the healthy persons. For ALT, AST, GGT, CK, LDH and HBDH, the average levels of the former were significantly higher than those of the later (P<0.05). Although the values of TP and of four patients were all in the reference range, both averages of them in patient group were all significantly higher than those in health group (P<0.05)

Discussion

As we known, the key disease caused by SARS-Cov-2 was pneumonia, and the patients generally exhibited respiratory symptoms including fever, cough, diarrhea, sore throat, dyspnea, and so on.(8,12) Along with more and deeper researches, scholars found that beside lung the, other organs or tissues were also injured in the course of COVID-19, such as heart, liver, kidney, and even the immune system.(3,13,14) What is more serious that part of the patients with COVID-19 finally died due to the multiple organ failure, shock, acute respiratory distress syndrome, heart failure, arrhythmias, or renal failure.(14,15) Therefore, beside pneumonia, the status of other organs should be paid more attention in the progress of diagnosing and treating COVID-19. In the present study, we collected the laboratory results of the patients with SARS-Cov-2 infection and accordingly assessed the effects of the coronavirus on several organs.

Liver function of COVID-19 patients

As shown in Table 1, many indices related to liver function were detected in four patients with COVID-19. The increase of ALT, AST, GGT in P2 and GGT in P3 indicated there the live function was abnormal for both patients. Overall, one in four of patients outranged for ALT and AST and the both abnormal rates were all 25%; this indicated that there were about a quarter of patients with COVID-19 suffering liver injury. These results were very consistent with Guan’s study⁷ in which the ratios of ALT and AST were 21.3% and 22.2%, respectively. However, the results of both studies differed from those of Chen’ team,(14) by whom the ratios of both indices were respectively reported as 28% and 35%. The reason for the gaps possibly laid on there were some severe or critical cases in the last report, while the patients in our study were belong to the common cases according to “Pneumonia Dianosis and Treatment Protocol for novel coronavirus (SRAS coronavirus 2 (SARS-Cov-2) infected pneumonia (trial version 5)”.(16) In another multicenter study,(17) the abnormal ratio for ALT was 21% which was very close near to this study. This consistency again proved that about one quarter of patients with mild COVID-19 had liver function abnormal.

Except for analyzing the laboratory results from the angle of reference range, we also compared the average of the indices between the patients with COVID-19 and those of the healthy

persons. As results shown in Table 2, the means of ALT, AST and GGT of patients were significantly higher than those of the healthy persons. This difference indicated that liver injury possibly was one of the clinical manifestations or complications in the patients with SARS-Cov-2 infection. (18,19)

Originally, TP values of the four patients were normal. It is interesting that the average of the index was significantly lower than that of the healthy persons, and this could be taken as another powerful evidence for liver function being affected by of SARS-Cov-2. As a protein synthesized in hepatocytes, PA concentration descended in three fourths of patients with COVID-19 in this study. This change was another evidence that live lesion was a relatively common phenomenon in the patients with infection of SARS-Cov-2. In a study on SARS, Jiang et al.(20) found that the concentrations of several proteins declined. Such a consistent finding probably indicated that the causative coronavirus could cause protein metabolic disorder.

So far, the detail mechanisms for liver injury caused by SARS-Cov-2 infection remain unknown. Some scholars thought this injury caused by the side effect of drugs which used to treat the COVID-19, especially the severe patients admitted in intense care unit.(21,22) However, the patients in our study did not accept systemic treatment before the infection was confirmed. Some researchers considered that the possible mechanism for abnormal liver function laid on the direct or indirect damage brought by the virus to hepatocytes.(22)

Heart function of COVID-19 patients

CK, LDH and HBDH were the indices used to assess the heart function. In this study, elevated CK, LDH and HBDH were found in P2 and P4; while only CK increased in P3. This probably represented that cardiac lesion always happened accompanying with COVID-19. However, the different increased indices and indices concentrations reflected that the extent of effect caused by SARS-Cov-2 probably was different in different individuals.

In other reports, some laboratory indices relative to heart function were also observed. Zhao et al.(23) observed 19 mild patients with COVID-19 and found the increase rate of LDH was 52.6%. Chan and his mates(24) investigated a family cluster of cases with COVID-19 and found 3 in 5 of persons had elevated level of LDH. Both reports shared the similar increase ratio for LDH with our study. In several researches which took CK as the important index to estimate heart function affected by SARS-Cov-2 infection, reported the increase rates of the index respectively were 13.7%, 33.0%, 13.0%.(3,7,14) However, these rates were obviously lower than 75% in our study, and the reason for the large gap probably because of the different population or case size.

In comparison with healthy persons, the averages of CK, LDH and HBDH were all much higher. This results indicated that cardiac damage probably was rather common in the patients with SARS-Cov-2 infection.(25) Meanwhile, the mean level of CK-MB of the patients was obviously lower than that of the health ones, which further proved that the high levels of CK, LDH and HBDH just originated from heart injury rather not other organs or tissues, such as muscles, brain, etc.

Beside biochemical indices, heart injury caused by infection of SARS-Cov-2 has also been proved by a report of pathological anatomy on a death case with COVID-19 until today.(26) As to the causative mechanism of SARS-Cov-2 to heart, there were mainly three aspects posed by scholar to date, namely, direct damage of coronavirus to cardiomyocyte,(27) injury induced by angiotensin converting enzyme 2 (ACE2) and it's receptor(3) and immunologic injury triggered by virus infection.(28) As to the complete theory about this still need further more studies and explorations.

Renal function of COVID-19 patients

In clinic, Cr, β 2-MG, BUR or blood urea nitrogen (BUN) were generally considered as the serologic markers reflecting the function of kidney. Ding and his colleagues (29) detected Cr and BUN concentrations of five patients with COVID-19 and found that both indices were all normal. This finding was in accordance with our study. This consistent results in two studies meant that it was necessary to kidney lesion for the patients with SARS-Cov-2 infection. Chen et al. (14) studied 99 cases with COVID-19 and found Cr increase ratio was about 3%; while in Xu's report,(30) there were 4 cases exhibited with rise of Cr in 19 patients with COVID-19 and the elevated rate was high to 21%. The higher ratio of abnormal renal function probably because some patients in these studies had kidney disease before SARS-Cov-2 infection. Therefore, it was uncertain that COVID-19 was responsible for abnormal renal function until any chronic kidney diseases could be ruled out.

Compared to lack powerful evidence for proving SARS-Cov-2 could cause damage to kidney, a study based on a contrite meta-analysis of early and preliminarily available data showed that chronic Kidney disease (CKD) seems to be associated with enhanced risk of severe COVID-19 infection.(10) Hence, it is suggested that the patients with CKD should be taken extra precaution to minimize risk exposure to the virus.

Glycaemic level of COVID-19 patients

Diabetes was presently reported as a one of the more common co-morbidities for COVID-19. In a study, diabetes was present in 42.3% of 26 fatalities due to COVID-19,(31) which showed the patients with diabetes were more prone to infecting SARS-Cov-2. In another study, 68 death in 150 patients from Wuhan showed that the number of diabetes co-morbidities to be a significant predictor of mortality for COVID-19 patients.(32) Even in a reference with a large size of 72,314 cases of COVID-19 published by Chinese Centre for Disease Control and Prevention also showed increased mortality in people with diabetes. (33) However, there was no direct evidence in all the reports to prove that SARS-Cov-2 infection or COVID-19 could cause the rise of glycaemic. In our study, the GLU contents of four patients were all in the normal range. These results perhaps told that there was no relation between blood glucose or diabetes and SARS-Cov-2 infection.(34) As to diabetes elevating the morbidity and mortality of patients with COVID-19,(35) the possible reason was that ACE2 expression increased in many diabetes patients who usually treated with some drugs,(36) or elevated glucose levels may serve to suppress the anti-viral immune response.(35) Based on such findings, glycaemic control or management of patients with COVID-19 should be better valued and optimized by physician.

Our study has several limitations. First, only four patients with SARS-Cov-2 infection are enrolled in and the sample size is small. This limited data probably bring bias for the analysis. Second, the dynamic changes of the laboratory results are not involved, and thus, the observation on continuous effects of SARS-Cov-2 to the function of multiple organs are absent. Third, virus load was not recorded, so the analysis of the possible correlations between virus load and changes of serological indices were missed.

Conclusions

In conclusion, infection of SARS-Cov-2 could cause liver and heart injury, while the effect of the virus on kidney and blood glucose metabolism is not observed in this study. Accordingly, we suggested that clinicians and researchers should pay more attention on the prevention, treatment and causative mechanism of the injury to multiple organs, such as liver and heart.

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Conflicting Interest

No conflict of interest

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