Characteristics and change patterns of liver function in 105 hospitalized adults patients with COVID-19 in Beijing, China

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Abstract

Background Previous studies showed that some coronavirus disease-2019 (COVID-19) patients might have some degree of liver biochemical abnormalities. However, no data on the stratified analysis and change patterns of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total bilirubin (TBil) have been reported.

Methods We performed a single-center, retrospective study. 105 hospitalized COVID-19 adults in Beijing Ditan Hospital from Jan. 12, 2020 to Mar. 17, 2020 were enrolled. Then we observed the characteristics and change patterns of ALT, AST, or TBil in the patients.

Results Ages of patients ranged 18-92 years old, with a median age of 43.4 years for mild ill group and 58.2 years for severe ill group (p < 0.001). The patients were hospitalized for a median of 22 days. 89 patients underwent abdominal ultrasound scans for fatty liver, with an overall proportion approximately 41.6%. 17 (16.2%) patients had abnormally elevated levels ALT. ALT and AST abnormalities occurred in 48.0% of severe ill group patients, compared to 13.9% of mild ill group. 19 (18.1%) patients showed ALT, AST and TBil levels ≥ 2 × ULN. 9 patients showed any index ≥ 3 × ULN. ALT, AST, and TBil levels ≥ 2 × ULN were observed in only 1 critically ill patient. All patients could be divided into 4 kinds of patterns based on the ALT index of baseline and hospitalization: Continuous normal (64.7%), normal and then abnormal (19.0%), abnormal and then normal (8.6%), continuous abnormal (7.6%).

Conclusion Although elevated liver function indexes are common in patients with COVID-19 infection, most non-severe ill patients only show mild abnormalities or transient increases.

Introduction

Coronavirus disease-2019 (COVID-19) is a new acute respiratory infectious disease. Its main characteristics are rapid transmission and general susceptibility of the population. The clinical manifestations are fever, dry cough and asthenia. Patients severely affected often experience dyspnea and/or hypoxemia in one week after onset, and the mortality rate is about 1% ~ 3% [1, 2]. In clinical practice and a small number of literature reports, some patients might have some degree of liver biochemical abnormalities, but most patients show only mild elevations of Alanine
aminotransferase (ALT) and/or aspartate aminotransferase (AST) that reflect hepatocellular damage[1]; patients with severe ill disease have a higher incidence of transaminase elevations than those with mild and common disease, and those requiring intensive care unit (ICU) admission, mechanical ventilation, or death have a significantly higher incidence of transaminase elevations than other patients[3, 4]. Till date, however, no data on the incidence of concurrent elevations of serum transaminases and total bilirubin(TBil) in patients with COVID-19 have been reported, and there are rare reports of increased transaminases stratification and comparative characteristics of dynamic changes over the course of the disease.

Methods

Study Design

This was a single-center, retrospective study. The subjects were patients diagnosed with COVID-19 who were admitted to Beijing Ditan Hospital, Capital Medical University, from January 12, 2020 to March 17, 2020. The patients were divided into mild ill (mild and ordinary types) and severe ill (severe and critical types) groups according to their condition. The clinical data and baseline liver biochemistry indexes were described and compared between the two groups.

Inclusion and Exclusion Criteria

Inclusion criteria: 1) Age≥18 years old and gender was not limited. 2) The diagnosis and classification of COVID-19 was based on the "New Coronavirus Pneumonia Diagnosis and Treatment Plan (Trial Edition 4-6)" published by the Chinese Health and Health Council. The diagnostic criteria are[2]: A. Mild type: Clinical symptoms were mild without pneumonia manifestation through image results; B. Ordinary type: Having fever and other respiratory symptoms with pneumonia manifestation through image results; C. Severe type: Meeting any one of the following: Respiratory distress, hypoxia (SpO2 ≤ 93%), abnormal blood gas analysis: (PaO2 250 mmHg); D. Critical type: Meeting any one of the following: Respiratory failure which requires mechanical ventilation, shock, accompanied by other organ failure that needs ICU monitoring and treatment. 3) All patients had nasal or pharyngeal swabs taken prior to admission, and tested positive by Real time PCR for the SARS-CoV-2 gene; all patients had a chest CT scan after admission. 4) Patients enrolled in the study had discharged or died by
March 17, 2020. 5) Discharge criteria: Normal hypothermia for more than 3 days; Resolution of respiratory symptoms; Chest computed tomography showed improvement in lung inflammation; Negative RT-PCR results for SARS-CoV2 respiratory samples at least 24 hours apart [2].

Exclusion criteria: 1) Age < 18 years old. 2) Patients who were still hospitalized in Beijing Ditan Hospital, Capital Medical University until March 17, 2020. 3) The patients did not have complete medical history, and in particular, liver function tests were not performed during the course of the disease.

**Data Collection**

The general information of all patients was collected, including gender, age, time of onset, hospitalization length, combined illness and drinking history. All patients underwent liver blood chemistry analysis at admission and were re-examined during hospitalization. Some patients underwent abdominal ultrasound examination results.

The normal range as follow: 1)ALT: male 9.0-50.0U/L, female 7.0-40.0U/L; 2) AST: male 15.0-40.0U/L, female 13.0-35.0U/L; 3) TBil: 18.8μmol/L; 4) albumin (ALB): 40.0-55.0g/L; 5) cholinesterase (CHE): 4000-11000U/L.

**Statistical Analysis**

All study data were described and analyzed using SPSS (Version 17.0). For metrological data, the distribution test was first performed, the mean ± standard deviation (mean ± SD) of the normal distribution data was selected for description, the difference between groups was compared using a t-test (with variance heterogeneity using corrected t-test), the median (interquartile range) of the metrological data for the skew distribution was expressed using a Wilcoxon rank sum test, and the difference between groups was compared using a Wilcoxon rank sum test. Count data are presented as frequency or rate, significance test is used χ² test. P < 0.05 was statistically significant.

**Results**

**Patient inclusion process diagram**

A total of 105 patients were included in this study, accounting for 52.8% of the patients diagnosed for COVID-19 at Beijing Ditan Hospital, Capital Medical University from January 12, 2020 to March 17,
2020, as shown in Figure 1.

Ages of patients ranged between 18 and 92 years old, with a median age of 43.4 years for mild ill group and 58.2 years for severe ill group (p < 0.001). Among 79 mild ill group cases, the ratio of male: female = 1:1. There were 26 severe ill cases, including 18 (69.2%) males and 8 (31.8%) females. The median number of illness days was 7.0 in severe ill group, which was significantly longer than the 4.0 days observed in the mild group. The patients were hospitalized for a median of 22 days, and 31.5 days for severe ill group, which was significantly longer than 20 days for mild ill group (refer to Table 1).

**Baseline characteristic analysis of all patients**

We analyzed the baseline data of 105 patients (Table 1). A total of 89 patients underwent abdominal ultrasound scans for fatty liver, with an overall proportion approximately 41.6%. The rate was 40.0% of mild ill group and 45.8% of severe ill group, with no statistically significant difference between the two groups (p = 0.62). Among 105 patients, only 1 patient had a long history of ethylalcohol content >40 g/day. All patients denied a history of chronic hepatitis B or chronic hepatitis C. HBsAg, anti-HCV, anti-HIV, and syphilis-specific antibodies detection during hospitalization was performed for 22 patients, but only 1 patient was anti-HCV positive without HCV RNA load.

The results of liver function indexes are shown in Table 1. ALT of all patients was measured of which 17 (16.2%) patients had abnormally elevated levels, with a median of 22.0 U/L for mild ill group and 27.8 U/L for severe ill group, with no statistically significant difference between them. One 45-year-old man had the highest ALT of 357 U/L among all patients. Unfortunately, only 50 patients were analyzed for AST, TBil, CHE, and ALB levels at admission. The results showed that the median of AST was 46.3 U/L for severe ill group which was significantly higher than 22U/L for mild ill group (p < 0.001). For TBil index, the median was 10.0μmol/L for mild ill group and 10.6μmol/L for severe ill group, with no statistically significant difference between the two groups (p = 0.54). CHE analysis did not show statistically significant difference between the two groups (p = 0.14). The median for ALB index was 42.0 g/L for the mild ill group, which was slightly higher than that observed in the severe ill group of 37.2 g/L (p = 0.012).
According to abdominal ultrasound diagnosis, 11 of 37 patients (29.7%) with fatty liver and elevated ALT. 6 (21.6%) were mild ill and 5 (13.5%) were severe ill. At least 9 of them were < 2 × ULN (Upper limit of normal value) and the highest was 129.9 U/L. We did not perform the statistical analysis considering the sample bias.

**Stratified Analysis of Baseline Liver Function Indexes**

The stratified analysis results of the abnormal elevated liver function indexes are presented in Table 2. A total of 22 (30.0%) patients showed abnormality in ALT or AST or TBil, including 14 (17.7%) patients in mild ill group and 30.8% in severe ill group. There was no statistically significant difference between the two groups (p = 0.156).

For single ALT index, the proportions between the mild and severe ill group were not statistically difference in all stratified comparison (p>0.05).

Interestingly, for the single AST index, the two groups showed a significant difference. 7 (63.6%) group cases experienced > 1 × ULN and 1 patient reached 87.7 U/L, while only 2 of the mild ill group cases (5.1%) had > 1 × ULN and no cases of ≥ 2 × ULN. A total of 50 patients were tested for TBil and only 2 patients of severe ill group had abnormalities, but all abnormalities were below 2 × ULN.

**Stratified and Joint Analysis of Liver Function Indexes during Hospitalization**

One critically ill patient died in this study, with a fatality rate < 1.0% in 105 patients. A total of 508 times ALT, 383 times AST, and 383 times TBil were collected, averaging 3.64-4.83 times for one patient during hospitalization.

Liver function indexes of all patients were observed dynamically according to the different combined models of ALT, AST, and TBil, as shown in Table 3.

At the single index analysis, the highest ALT was 357 U/L, AST was 156.3 U/L, and TBil was 102.9 μmol/L. 56.2% of 105 patients had abnormality with single index, and rate was up to 69.2% in severe ill group, significantly higher than that of 51.9% in mild ill group (p < 0.001); ALT and AST abnormalities occurred in 48.0% of severe ill group patients, compared to 13.9% of mild ill group. However, 19 (18.1%) patients showed ALT, AST and TBil levels ≥ 2 × ULN, of which 10 patients were from the severe ill group cases, significantly higher than mild ill group cases. 9 patients showed any
index ≥ 3 × ULN. The proportion of elevated TBil with elevated AST was higher than with elevated ALT.

In the combined indexes analysis, ALT or AST associated with TBil and 3 indexes elevations together were more common in severe ill group patients (p < 0.001); However, only 8 patients numerically were seen with an increase in the 3 indexes together, 7 of whom were severe ill group cases. Furthermore, ALT, AST, and TBil levels ≥ 2 × ULN were observed in only 1 critically ill patient. These results suggest that during the course of COVID-19, liver function abnormalities are generally mild, and moderate and severe liver injury is very low.

**Patterns analysis of liver function indexes during hospitalization**

We divided all patients into 4 kinds of patterns based on the ALT index of baseline and hospitalization: Continuous normal, normal and then abnormal, abnormal and then normal,continuous abnormal. The results are shown in Table 4.

In total, 68 patients (64.7%) had normal ALT during the course of COVID-19, 12 patients (46.2%) were severe ill group cases and 56 patients (70.9%) were mild ill group cases, which was significantly higher than that of the former (p = 0.022).

Twenty (19.0%) patients had normal ALT at admission but had abnormalities during hospitalization of which 9 (34.6%) patients were severe ill group cases and 11 (13.9%) patients were mild ill group cases(p = 0.009). By the time the last test was done before discharge, 10 mild ill group patients still had ALT abnormalities, 3 of which were > 2 × ULN. Most of ALT elevations occurred between day 4 and day 17 of hospitalization, with a mean of 7.3 ± 3.0 days for severe illgroup and 10.7 ± 4.1 days for mild ill group, with significant differences between the two groups (p = 0.048); Excluding 1 patient who delayed detection for personal reasons, ALT assessments were performed every 2.7 ± 0.6 days between admission and the onset of ALT elevations in mild ill group,and 2.6 ± 0.7 days in severe ill group. There was no significant difference between the two groups (p = 0.86), suggesting that the finding of ALT elevations was not related to delayed detection in mild illgroup.

Nine patients (8.6%) had elevated ALT at admission but continued to decline until recovery during the subsequent treatment period; 7 patients (8.9%) were mild ill group cases and 2 patients (8.0%) were
severe ill group cases, with no statistically significant difference between the two groups (p > 0.99).

Eight patients (7.6%) had abnormal ALT at admission, followed by continuous abnormality or fluctuation in normal/abnormal state; 5 patients (6.3%) were mild ill group cases and 3 patients (11.5%) were severe ill group cases. At the last test in these patients, 5 patients still failed to show normalized ALT, suggesting that they should be analyzed for other causes of transaminase elevations.

An observation on the dynamic Change of ALT in a mild ill patient

We also focused on the outcome of one mild ill patient with baseline ALT > 7 × ULN. A 45-year-old male patient, who denied a long history of heavy alcohol use and chronic liver disease, presented with cough, fever, and chills on Jan. 24, 2020 and was admitted to the hospital on Jan. 28, 2020 with a diagnosis of COVID-19. After admission, ALT 357 U/L was found. Abdominal ultrasound showed no fatty liver, and HBsAg and anti-HCV were negative. Antipyretic, nutritional support, recombinant human interferon α-2b, lopinavir ritonavir tablet and reduced glutathione, compound glycyrrhizin were administered. During the treatment, the patient's ALT gradually returned to normal (as shown in Figure 2), and the patient's sputum samples were serially negative for SARS-CoV-2 on Feb. 10, 2020 and Feb. 12, 2020, and he was discharged.

Discussion

COVID-19 is a new kind of infectious disease, so there are only limited reports about liver injury. All the data was from observational clinical studies, and the information to understand the underlying liver disease and medicine use is limited.

In order to better show the dynamic changes of liver function indicators of patients throughout the course of the disease, we selected patients who had been discharged or died as research subjects. Therefore, a total of 105 adult patients were included in the study. Compared with patients in the mild ill group, the mean age of the severe ill group patients was older, the number of days of onset was longer, and the proportion of men was larger, which is consistent with the previous reports [5]. Among 105 patients, 40.0% of patients in mild ill group and 45.8% of patients in severe ill group had fatty liver, which was also roughly equal to that of the general population [6], suggesting that fatty liver might not be a predisposing factor for COVID-19.
At present, COVID-19 associated liver biochemistry abnormality is believed to be responsible for direct liver cells injury [7], drug-induced liver injury [1, 8], hypoxic-ischemic microcirculation disorder, and underlying liver diseases. Temporal relationship is an important clue in the identification of viral direct injury and drug-induced liver injury, whereas hepatic injury associated with hypoxic-ischemic microcirculation disorder may be more common in critically ill patients. This study found that up to 56.7% of patients had abnormal elevations of ALT, AST, or TBil throughout the course of COVID-19, and 26.7% occurred after admission. AST is widely distributed in muscle, cardiac myocytes and mitochondria, so a single index of AST could not be considered to represent abnormal liver biochemistry. It is often necessary to conduct joint analysis with ALT and TBil. In this study, the rate of ALT and TBil abnormalities in all patients was less than 20.0%, but in the severe ill group the rate of AST abnormalities was 63.6%, ALT and AST elevated together was 48.0%, and especially the rate of ALT and AST combined with TBil increased 28%, which was significantly higher than that of mild ill type. Since COVID-19 patients might have exudative lesions in the lungs, poor nutritional intake after onset, and poor nutritional status in the elderly, although it was observed in this study that the reduction in albumin was higher in critically ill patients than in mild ill patients at admission, it was not considered to be related to severe impairment of liver function. We also focused on the changes in liver function during the course of COVID-19. Stratified and joint analysis showed that 56.2% of COVID-19 patients had elevated ALT, AST, or TBil levels during the course of COVID-19. The percentage of elevated TBil was 20.8% for mild ill group, 36.0% for severe ill group, and they were both significantly higher than the previous report (9.8% and 20.8%) [1]. One patient with an unknown cause had ALT as high as 7590 U/L in previous report [5], but the highest ALT in this study was only 357 U/L. Fortunately, the incidence of a combined increase of 3 indexes in all patients was very low at 7.6%; Only 1 patient was critically ill with all 3 indexes≥2×ULN. At the same time, we focused on the outcome of one of the highest ALT levels in the study, with a good recovery of liver injury in the course of treatment. These results suggest that COVID-19 patients are mildly impaired, although a significant proportion have elevated liver function parameters; Even if there is more than moderate impairment, if other systems are functioning well, the overall condition
is less severe, and liver function can be better restored.

In an analysis of the etiology of hepatic impairment in patients with COVID-19, we also performed a preliminary study. We divided the ALT levels into four change patterns: continuous normal, normal and then abnormal, abnormal and then normal, continuous abnormal. 68 patients were found to have continuous normal ALT during the course of the disease. Eight patients belonged to the continuous abnormal pattern, and 5 patients failed to return to normal at last test. Considering the mechanism of COVID-19 liver injury, we concluded that these patients might need additional relevant testing to look for underlying causes for liver biochemistry abnormality. Most of these patients had ALT elevations between days 4 and 17 of hospitalization, with a mean of 7.3 days for severe ill patients and 10.7 days for mild ill patients. We also confirmed that there was no statistical difference between the two groups in the mean frequency of testing for the time period from baseline to the development of ALT abnormalities, thus excluding bias caused by more tests in critically ill patients. Overall, therefore, it is clear that severe ill group patients develop abnormal ALT earlier than mild ill group patients. It has been shown that patients with COVID-19 might fall in the mild ill group in the early stages, but developed further symptoms and worsened in about one week[1], so ALT abnormalities in these patients require further exploration, such as drug-induced liver injury[8] or associated with changes in disease status.

In conclusion, although elevated liver function indicators are more common in patients with COVID-19 infection, most patients have mild abnormalities or transient increases in individual indicators. Overall, liver damage was mild in patients with COVID-19 infection.

This study had some limitations. First, this study is a retrospective analysis of a single center. Second, while it has been postulated that novel coronaviruses can enter bile duct epithelial cells through ACE2 receptors to cause liver injury[9], but ALP and GGT were not been significantly elevated[10]. This study was unable to provide data on ALP and GGT due to conditions. Third, some patients had used antipyretic and analgesic drugs, antibiotics and other drugs before admission, and even most of the patients had been treated with multiple drugs during their stay in hospital. The specific dosage, type, and days of administration are not clear, which may affect the results. Fourth, some patients with
hypertension, coronary heart disease, type 2 diabetes mellitus, hypothyroidism and chronic obstructive pulmonary disease, and other similar chronic conditions were already on daily medication, and this may also have some impact on baseline indicators.

**Conclusion**

Although elevated liver function indexes are common in patients with COVID-19 infection, most non-severe ill patients only show mild abnormalities or transient increases.

**Declarations**

**Ethics approval and consent to participate**

This study has been approved by the Ethics Committee of Beijing Ditan Hospital Capital Medical University (number: 2020-010-01).

**Consent for publication**

Not applicable.

**Availability of data and materials**

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

**Competing interests**

The authors declare that they have no competing interests.

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**Author contributions statement**

W.X. and Q.W. conceived and designed the study; H.Z, LG.L., YB.W., T.Z., MH.L., YL.X., GJ.G., HF.X., Y.F., Y.C., R.D., JJ.W. and C.C. had roles in clinical management, patient recruitment, formulated the treatment regimens; Q.W., H.Z., and LG.L., contributed to data collections and data entry. Q.W. performed the statistics; Q.W. and W.X. also wrote the manuscript. All authors reviewed and approved the final version of the manuscript.

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Tables

Table 1. Baseline Characteristic Analysis of COVID-19 Patients
|                | Overall        | Mild ill group | Severe ill group | P-value |
|----------------|----------------|----------------|------------------|---------|
| Male (%)       | 56 (53.3%)     | 38 (48.1%)     | 18 (69.2%)       |         |
| (n=105)        | (n=79)         | (n=26)         |                  |         |
| Age (years),   | 45.0 [33.5, 59.5] | 41.0 [33.0, 56.0] | 59.0 [48.5, 69.8] | < 0.001 |
| median [Q1, Q3]| □n=105□        | □n=79□         | □n=26□           |         |
| Day of onset (days), | 5.0 [3.0, 8.0] | 4.0 [2.0, 7.0] | 7.0 [5.0, 10.25] | > 0.05  |
| median [Q1, Q3]| □n=105□        | □n=79□         | □n=26□           |         |
| Hospitalization| 22.0 [17.0, 31.5] | 20.0 [16.0, 28.0] | 31.5 [22.5, 35.5] | > 0.05  |
| length (days), | □n=105□        |                 |                  |         |
| median [Q1, Q3]|               |                 |                  |         |
| fatty liver by ultrasound (%) | 37 (41.6%) | 26 (40.0%) | 11 (45.8%) |         |
| (n=89)         | (n=65)         | (n=24)         |                  |         |
| Hypertension, %| 15 (14.3%)     | 9 (11.4%)      | 6 (23.1%)        |         |
| (n=105)        | (n=79)         | (n=26)         |                  |         |
| Diabetes, %    | 6 (5.7%)       | 3 (3.8%)       | 3 (11.5%)        |         |
| (n=105)        | (n=79)         | (n=26)         |                  |         |
| HBsAg (+)      | 0 (0)          | 0 (0)          | 0 (0)            |         |
| (n=22)         | (n=14)         | (n=8)          |                  |         |
| Anti-HCV (+)   | 1 (0)          | 0 (0)          | 1 (12.5%)        |         |
| (n=22)         | (n=14)         | (n=8)          |                  |         |
| Long history of heavy alcohol use (%) | 1 (1.0%) | 1 (1.3%) | 0 (0) | > 0.05 |
| (n=105)        | (n=79)         | (n=26)         |                  |         |
| ALT (U/L),     | 23.5 [14.0, 36.0] | 22.0 [14.0, 34.5] | 27.8 [18.8, 38.0] | (n = 26) |
| median [Q1, Q3]| □n=105□        | □n=79□         | □n=26□           |         |
| AST (U/L),     | 24.2 [19.7, 34.8] | 22.0 [18.4, 31.7] | 46.3 [25.5, 54.3] | (n = 11) |
| median [Q1, Q3]| □n=50□         | □n=39□         | □n=11□           |         |
| TBil (umol/L), | 10.2 [7.4, 12.9] | 10.0 [7.1, 12.9] | 10.6 [8.3, 12.9] | (n = 11) |
| median [Q1, Q3]| □n=50□         | □n=39□         | □n=11□           |         |
| CHE (U/L),     | 7490.0 [6801.0, 9527.0] | 6517.0 [6843.0, 9682.0] | 6972.0 [4893.0, 8459.0] | (n = 11) |
| median [Q1, Q3]| □n=50□         | □n=39□         | □n=11□           |         |
| ALB (g/L),     | 41.6 [37.9, 44.7] | 42.0 [38.7, 45.5] | 37.2 [34.2, 41.8] | (n = 10) |
| median [Q1, Q3]| □n=49□         | □n=39□         | □n=10□           |         |
|                | Overall | Mild ill group | Severe ill group |    |
|----------------|---------|----------------|-----------------|----|
| **ALT**        |         |                |                 |    |
| < 1 ×ULN       | n=105   | n=79           | n=26            |    |
|                | 88 (    | 67 (76.1%)     | 21 (80.8%)      | 0.62|
|                | 77.2%   |                |                 |    |
| ≥1 ×ULN        |         |                |                 |    |
|                | n=50    | n=39           | n=11            |    |
| ≥ 2 × ULN      | 4 (3.8%)| 2 (2.5%)       | 2 (7.7%)        | 0.26|
| ≥ 3 × ULN      | 3 (2.9%)| 2 (2.5%)       | 1 (3.8%)        | >0.99|
| ≥5 × ULN       | 1 (1.0%)| 1 (1.3%)       | 0 (0)           | >0.99|
| **AST**        |         |                |                 |    |
| < 1 ×ULN       | n=50    | n=39           | n=11            |    |
|                | 41 (    | 37 (94.9%)     | 4 (36.4%)       | <0.001|
|                | 82.0%   |                |                 |    |
| ≥1 ×ULN        |         |                |                 |    |
| ≥ 2 × ULN      | 1 (2.0%)| 0 (0)          | 1 (9.1%)        | 0.22|
| ≥ 3 × ULN      | 0 (0)   | 0 (0)          | 0 (0)           | /   |
| **TBil**       |         |                |                 |    |
| < 1 ×ULN       | n=50    | n=39           | n=11            |    |
|                | 48 (    | 38 (97.4%)     | 10 (90.9%)      | 0.40|
|                | 96.0%   |                |                 |    |
| ≥1 ×ULN        |         |                |                 |    |
| ≥ 2 × ULN      | 0 (0)   | 0 (0)          | 0 (0)           | /   |
| ALT or AST or TBil | n=105 | n=79           | n=26            |    |
| ≥1 ×ULN        | 22 (    | 14 (17.7%)     | 8 (30.8%)       | 0.16|
|                | 30.0%   |                |                 |    |
|                | Overall | Mild ill group | Severe ill group | P-value |
|----------------|---------|----------------|-----------------|---------|
| **ALT**        |         |                |                 |         |
| n=105          | n=79    | n=26           |                 |         |
| ≥1 × ULN       | 40 (38.1%) | 25 (31.6%)    | 15 (57.7%)     | 0.018   |
| ≥ 2 × ULN      | 15 (14.4%) | 8 (10.1%)     | 7 (28.0%)      | 0.06    |
| ≥ 3 × ULN      | 7 (6.7%)  | 5 (6.3%)       | 2 (7.7%)       | > 0.99  |
| ≥5 × ULN       | 2 (2.0%)  | 2 (2.6%)       | 0 (0)          | > 0.99  |
| **AST**        |         |                |                 |         |
| n=97           | n=72    | n=25           |                 |         |
| ≥1 × ULN       | 33 (34.0%) | 17 (23.6%)    | 16 (64.0%)     | < 0.001 |
| ≥ 2 × ULN      | 9 (9.3%)  | 4 (5.6%)       | 5 (20.0%)      | 0.08    |
| ≥ 3 × ULN      | 2 (2.1%)  | 1 (1.4%)       | 1 (4.0%)       | 0.45    |
| ≥5 × ULN       | 0 (0)    | 0 (0)          | 0 (0)          | /       |
| **TBil**       |         |                |                 |         |
| n=97           | n=72    | n=25           |                 |         |
| ≥1 × ULN       | 24 (24.7%) | 15 (20.8%)    | 9 (36.0%)      | 0.13    |
| ≥ 2 × ULN      | 4 (4.1%)  | 0 (0)          | 4 (16.0%)      | 0.004   |
| ≥ 3 × ULN      | 2 (2.1%)  | 0 (0)          | 2 (8.0%)       | 0.06    |
| ≥5 × ULN       | 2 (2.1%)  | 0 (0)          | 2 (8.0%)       | 0.06    |
| **ALT&AST**    |         |                |                 |         |
| n=105          | n=79    | n=26           |                 |         |
| ≥1 × ULN       | 22 (21.0%) | 10 (12.7%)    | 12 (46.2%)     | 0       |
|                  | ALT & TBil |       |       |       |       |
|------------------|------------|-------|-------|-------|-------|
|                  | n=105      | n=79  | n=26  |       |       |
| ≥ 1 × ULN        | 9 (8.5%)   | 2 (2.5%) | 7 (26.9%) | 0.001 |
| ≥ 2 × ULN        | 1 (1.0%)   | 0 (0)  | 1(3.8%) | 0.25  |
| ≥ 3 × ULN        | 0          | 0      | 0      | /     |

|                  | AST & TBil |       |       |       |       |
|------------------|------------|-------|-------|-------|-------|
|                  | n=97       | n=72  | n=25  |       |       |
| ≥ 1 × ULN        | 9 (9.3%)   | 1/72 (1.4%) | 8/25 (32.0%) | 0     |
| ≥ 2 × ULN        | 2 (1.0%)   | 0 (0)  | 2 (3.8%) | 0.25  |
| ≥ 3 × ULN        | 0          | 0      | 0      | /     |

|                  | ALT & AST & TBil |       |       |       |       |
|------------------|------------------|-------|-------|-------|-------|
|                  | n=105            | n=79  | n=26  |       |       |
| ≥ 1 × ULN        | 8 (7.6%)         | 1 (1.3%) | 7 (26.9%) | 0     |
| ≥ 2 × ULN        | 1 (1.0%)         | 0 (0)  | 1(3.8%) | 0.25  |
| ≥ 3 × ULN        | 0                | 0      | 0      | /     |

|                  | ALT/AST/TBil |       |       |       |       |
|------------------|--------------|-------|-------|-------|-------|
|                  | n=105        | n=79  | n=26  |       |       |
| ≥ 1 × ULN        | 59 (56.2%)   | 41 (51.9%) | 18 (69.2%) | 0.12  |
| ≥ 2 × ULN        | 19 (18.1%)   | 9 (11.4%) | 10 (38.5%) | 0.005 |
| ≥ 3 × ULN        | 9 (8.6%)     | 5 (6.3%)  | 4 (15.4%) | 0.30  |
|                  | Overall n=105 | Mild ill group n=79 | Severe ill group n=26 | P-value |
|------------------|---------------|---------------------|-----------------------|---------|
| Continuous normal| 68 (64.8%)    | 56 (70.9%)          | 12 (46.2%)            | 0.022   |
| normal and then abnormal | 20 (16.0%) | 11 (11.1%) | 9 (34.6%) | 0.009 |
| abnormal and then normal | 9 (8.6%) | 7 (8.9%) | 2 (7.7%) | > 0.99 |
| continuous abnormal | 8 (7.6%) | 5 (6.3%) | 3 (11.5%) | 0.66 |

Figures
From January 12, 2020 to March 17, 2020, 199 patients were admitted to Beijing Ditan Hospital.

124 patients were discharged and 1 patient died of COVID-19.

Age < 18 years old (n=15)

Age ≥ 18 years old (n=109)

Data imcomplete (n=4)

105 patients were enrolled into this study

mild ill group (n=79)

severe ill group (n=26)

Figure 1
The Flow of Patient Enrollment
Figure 1

Dynamics of liver function indexes in 1 mild ill patient with ALT elevation