Original Article

Analysis of occurrences and causes of abnormal liver function in 109 patients with COVID-19

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Abstract

Context: COVID-19 is a novel coronavirus pneumonia, which is related to abnormal liver function. Thus, it is important to explore the occurrences and causes of abnormal liver function with COVID-19. **Methods:** We chose 109 patients with COVID-19 in 2020 and studied the relationship between gender, age, basic diseases, antiviral drug treatment, disease classification, and abnormal liver function, and analyzed the causes of abnormal liver function in patients with COVID-19. **Results:** Among patients, 46 (42.20%) had abnormal liver function at admission; 37 (80.43%) had mild abnormal liver function; and 9 (19.57%) had severe liver function. Compared with other age groups, the abnormal rate of serum ALP in the group younger than 21 years old were the highest ($P < 0.05$). The abnormal rates and concentrations of serum ALT, AST and γ-GT in the male groups were higher than in female groups ($P < 0.05$), basic disease group were higher than those in the non-basic disease group ($P < 0.05$). Serum γ-GT concentration after 1 week of antiviral treatment was higher than that before treatment ($P < 0.05$). The abnormal rate of ALT and AST at discharge was lower than that after antiviral treatment for 1 week ($P < 0.05$). Serum TB and AST concentrations at discharge were lower than those before treatment ($P < 0.05$). Serum AST and γ-GT concentrations in severe/critical type group were higher than those in mild or ordinary type group ($P < 0.05$). **Conclusions:** In this study, we found male sex, basic diseases, antiviral drugs, and severe/critical types are related to the occurrence of abnormal liver function in COVID-19 patients.

Keywords: COVID-19, liver function, SARS-CoV-2

Introduction

The 2019 novel coronavirus disease (COVID-19) is a novel coronavirus pneumonia caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).[1] The main target organ of SARS-CoV-2 is the lungs; therefore, the most common symptoms in the clinic are respiratory symptoms such as cough, expectoration, and dyspnea.[2] SARS-CoV-2 can also invade multiple organs, such as the gastrointestinal tract, liver, kidneys, heart, and even skin,[3] and has multi-system and multi-organ clinical manifestations.[4]

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Abnormal liver function in patients with COVID-19 is relatively common and has become a prominent clinical problem.[4] However, the exact cause of liver dysfunction in COVID-19 patients remains unclear. This study collected data on 109 patients with COVID-19 admitted to Zhuzhou and Hengyang, studied the relationship between sex, age, basic diseases, antiviral drug treatment, disease classification, and abnormal liver function in patients with COVID-19, and analyzed the causes of abnormal liver function in patients with COVID-19. This study provides a theoretical basis for family physicians to identify and treat liver dysfunction in patients with COVID-19.

Patients and Methods

Patients

In 2020, 128 COVID-19 patients were diagnosed and treated in Hengyang and Zhuzhou cities, China, all of whom met the diagnostic criteria[5] in the novel coronavirus Diagnosis and Treatment Plan (Trial Seventh Edition) promulgated by the National Health and Health Commission, excluding patients with incomplete clinical data, the final number of cases included was 109.

Data collection

This was a retrospective study using the in-hospital electronic medical record system to obtain general data and laboratory data on patients, including epidemiological characteristics (gender, age), antiviral status, basic diseases, such as hypertension, coronary heart disease, diabetes, hyperlipidemia, gout, hyperthyroidism, chronic bronchitis, chronic obstructive pulmonary disease, chronic viral hepatitis B and lipid liver), COVID-19 patient classification, white blood cell (WBC), neutrophil (NEU), lymphocyte (LYM), and monocyte (MON) counts in whole blood, serum D-dimer and C-reactive protein concentrations, serum total bilirubin (TB), alanine aminotransferase, ALT, aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (γ-GT) concentrations before treatment, 1 week after antiviral treatment, and before discharge. Routine blood tests were performed using an automated hematology analyzer produced by Xisen Meikang Medical Electronics Co., Ltd. Blood biochemistry was detected using an automatic biochemical analyzer (Roche). This study does not interfere with the clinical treatment of patients and poses any risks to their physiology.

Diagnostic criteria of abnormal liver function

The diagnostic criteria for abnormal liver function combined with the American Hepatology Society (ACG), the British Gastroenterology Society (BSG), and China's Prevention, Diagnosis and Treatment of Novel Corona Virus Pneumonia with Liver Damage, which define any other liver biochemical index in ALT, AST, ALP, γ-GT, TB above the upper limit of normal (ULN) as abnormal liver function; any index of the liver biochemical index in ALT and AST is higher than ULN and less than 3 × ULN, or any liver biochemical index in TB, ALP, γ-GT is higher than ULN and less than 2 × ULN is mild liver abnormalities; any other liver biochemical index in ALT and AST is higher than 3 × ULN or ALP, γ-GT, and TB. A liver biochemical index higher than 2 × ULN is a severe liver function abnormality.[6-9] ALT and AST are mainly present in liver cells. An increase in ALT and AST levels represents liver cell injury, which is an abnormal liver cell-type liver function. When any index in TB, ALP, or γ-GT is increased, it represents bile duct cell damage, which manifests as cholestatic liver function abnormalities. When there is an indicator of ALT, AST, and an indicator of TB, ALP, and γ-GT, both hepatocytes and bile cells are damaged and bile cells are damaged, indicating mixed-type damage.[10]

Statistical methods

SPSS26.0 software is used to conduct statistical analysis of data. Data are represented as percentages (n/N). When comparing multiple sets of data, the inspection level was adjusted using the Bonferroni method to avoid the occurrence of Class I errors. In this study, the measured data were subject to abnormal distribution. Expressed by median digits (interquartile spacing), that is, M (interquartile range [IQR]), non-parametric tests (Mann–Whitney test or Wilcoxon test or Kruskal–Wallis test); $P < 0.05$ is considered statistically significant; the graph is made using GraphPad Prism 6 software.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Result

Relationship between age and abnormal liver function in COVID-19 patients

The average ± standard deviation of the age of selected patients was 43.6 ± 17.8 years, the median age was 41 years, the oldest was 88 years old, and the minimum age was 3 years. The selected patients were divided into four groups by age: less than 21 years old (9.2%), 21–40 years old (35.8%), 41-60 years old (33.0%), and more than 60-year-old group (22.0%). Biochemical indicators can be measured according to counting data, and row × column card can be carried out. The results showed that the TB, ALT, AST, and gamma-GT indicators had no statistical significance; the ALP indicators were statistically significant, indicating that the ALP abnormality rate varies among different age groups. As shown in Figure 1a, to avoid the occurrence of Class I errors, it was found that the abnormal rate of ALP in patients younger than 21 years old was the highest compared with other age groups after correction, and the difference was statistically significant ($P < 0.05$). Biochemical indicators can be measured using counting data, and Kruzkal-Wallis tests can be carried out. TB, ALT, AST, and gamma-GT indicators had no statistical significance. After correction by the same method as above, it was found that compared with other age groups, as shown in

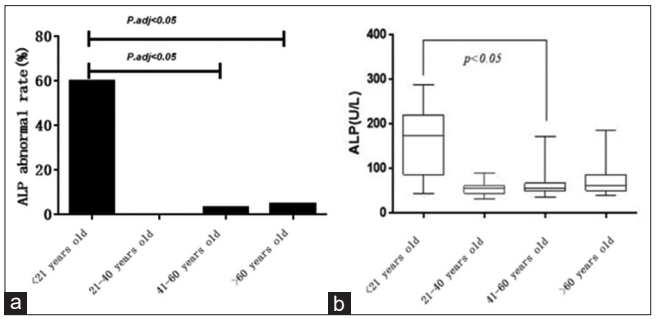

Figure 1: a: abnormal rate of ALP in each age group. b: median and interquartile distance of ALP in each age group

Figure 1b, the serum ALP concentration of patients younger than 21 years old was higher than that of patients aged 41–60 years old, and the difference was statistically significant ($P < 0.05$).

Relationship between gender and abnormal liver function in COVID-19 patients

A total of 109 patients with COVID-19 met the inclusion criteria and were divided into male and female groups according to sex: 58 male patients (53.2%) and 51 female patients (46.8%). As shown in Table 1, biochemical indicators were counted according to the count, and the two groups were tested using the card prescription. The results showed that the TB and ALP indicators were not statistically significant, and the abnormal rates of ALT, AST, and gamma-GT in the male group were significantly higher than those in the female group ($P < 0.05$). As shown in Table 2, the biochemical indicators were statistically measured according to the measured data. The two sets of data were subject to an unipositive distribution, and the Mann–Whitney test was performed. The results show that The ALP index was not statistically significant. The concentrations of serum TB, ALT, AST, and gamma-GT in the male group were greater than those in the female group, and the difference was statistically significant ($P < 0.05$).

Laboratory results of abnormal liver function in COVID-19 patients

Before treatment, COVID-19 patients had 46 patients had abnormal liver function (42.20%), including 37 patients with mildly abnormal liver function (80.43%) and 9 patients with severely abnormal liver function (19.57%). Among the patients, 28 (60.87%) were complicated with basic diseases, and 18 (39.13%) were COVID-19 patients without basic diseases. In addition, COVID-19 patients without basic diseases have not used any drugs, and there is no cause or inducement of abnormal liver function, except for SARS-CoV-2.

Patients were divided into normal and abnormal liver function groups. As shown in Tables 3 and 4, after removing the patients with no data from the laboratory results, the two groups were compared, and the C-reactive protein (CRP), leukocyte count (WBC), neutral granulocyte count absolute value (NEU), lymphocyte count absolute value (LYM), single nucleocyte count absolute value (MON), D-dimer (D-D) according to the counting data and measurement data, and the card test and Mann–Whitney test, respectively, were not statistically significant.

Table 1: Comparison of abnormal rates of biochemical indicators between male and female patients [%(*n*/*N*)]

	Male	Female	χ^2	*P*
TB	8.62 (5/58)	7.84 (4/51)	-	1.000
ALT	34.48 (20/58)	7.84 (4/51)	11.216[a]	0.001*
AST	24.14 (14/58)	5.82 (3/51)	6.870[a]	0.009*
ALP	11.54 (6/52)	4.76 (2/42)	-	0.291
γ-GT	21.15 (11/52)	4.76 (2/42)	5.239[a]	0.022*

Note: In the table, % represents the abnormal rate of biochemical indicators in each group; n represents, the number of cases with abnormal biochemical indicators in each group, and *N* represents the total number of cases in each group; [a]indicates that the expected count of 0 cells is <5; χ^2 is the Chi-square value; *means *P*<0.05, which is statistically significant

Table 2: Median Comparison of Biochemical Index Concentration between Male and Female Patients [M (IQR)]

	Male	Female	*Z*	*P*
TB umol/L, M (IQR)	11.02 (8.19~16.24)	8.31 (5.18~12.60)	-2.706	0.007*
ALT U/L, M (IQR)	26.05 (17.88~45.55)	15.30 (11.40~22.60)	-4.137	0.000*
AST U/L, M (IQR)	26.85 (22.73~36.00)	22.00 (18.20~27.00)	-3.278	0.001*
ALP U/L, M (IQR)	58.00 (51.00~75.75)	58.00 (45.75~76.00)	-0.803	0.422
γ-GT U/L, M (IQR)	28.50 (18.30~46.25)	17.00 (11.75~28.25)	-3.314	0.001*

Note: In the table, M represents the median and IQR represents the interquartile distance; *Z* is the test statistic of the Mann-Whitney test; *indicates *P*<0.05, which is statistically significant

Table 3: Comparison of abnormal rate of laboratory indicators between patients with normal liver function and patients with abnormal liver function [%(*n*/*N*)]

	Normal liver function	Abnormal liver function	χ^2	*P*
CRP normal	54.55 (30/55)	51.43 (18/35)	0.083[a]	0.773
Increased	45.45 (25/55)	48.57 (17/35)		
WBC normal	52.46 (32/61)	68.18 (30/44)	3.164[a]	0.206
Decreased	44.26 (27/61)	27.27 (12/44)		
Increased	3.28 (2/61)	4.55 (2/44)		
NEU normal	66.67 (40/60)	72.73 (32/44)	1.121[a]	0.571
Decreased	26.67 (16/60)	18.18 (8/44)		
Increased	6.67 (4/60)	9.09 (4/44)		
LYM normal	83.33 (50/60)	75.00 (33/44)	2.069[a]	0.355
Decreased	16.67 (10/60)	22.73 (10/44)		
Increased	0	2.27 (1/44)		
MON normal	97.44 (38/39)	93.55 (29/31)	-	0.580
Decreased	2.56 (1/39)	6.45 (2/31)		
D-D normal	80.36 (45/56)	84.44 (38/45)	0.285[a]	0.594
Increased	19.64 (11/56)	15.56 (7/45)		

[a]Note: In the table,%, *n*, *N* and χ^2 indicate the same meanings as Table 1; a indicates that the expected count of 0 cells is <5

Relationship between basic diseases and abnormal liver function in COVID-19 patients

The selected patients were divided into two groups: those with basic diseases and those with non-basic diseases. Patients in the

group with basic diseases refer to the merger of one or more basic diseases, including hypertension, coronary heart disease, diabetes, hyperlipidemia, gout, hyperthyroidism and subtraction, chronic bronchitis, chronic obstructive pulmonary disease, chronic viral hepatitis B, and lipid liver. There were 55 patients with one or more basic diseases, of which the first three were hypertension, chronic liver disease, and diabetes, of which 19 (42.22%), 19 (42.22%), and 10 (22.22%) had non-basic diseases, respectively. There are 54 cases. After relevant statistics, it was found that the probability of mild liver dysfunction in the basic disease group and the non-basic disease group was 43.6% and 31.5%, respectively, and the probability of severe liver dysfunction was 7.3% and 5.6%, respectively. Patients with severe liver dysfunction have increased TB, ALP, and gamma-GT levels, and most of the two groups showed mild liver abnormalities.

As shown in Table 5, according to the above method, the two groups were tested on a card prescription basis. TB, ALP and gamma-GT were not statistically significant. The abnormal rates of ALT and AST in the basic disease group were significantly higher than those in the baseless disease group ($P < 0.05$). As shown in Table 6, according to the above method, the Mann–Whitney test was not statistically significant for the TB and ALP indicators; the serum ALT, AST, and gamma-GT concentrations in the basic disease group were greater than those in the non-basic disease group, and the difference was statistically significant ($P < 0.05$). As shown in Table 7, the top three diseases in terms of incidence of basic diseases were divided into three groups: Chronic liver disease, hypertension, and diabetes. The number of abnormal biochemical indicators in each group was counted, and the three groups were tested using row × column card prescriptions. The results show that each biochemical index was not statistically significant. As shown in Table 8, the three sets of data obey the abnormal distribution and are tested using Kruskal-Wallis. The results showed that none of the biochemical indicators were statistically significant.

Table 4: Comparison of abnormal median concentration of laboratory indexes between patients with normal liver function and patients with abnormal liver function [M (IQR)]

	Normal liver function	Abnormal liver function	*Z*	*P*
CRP mg/L, M (IQR)	7.3 (5.0~17.7)	8.9 (5.0~25.7)	-0.067	0.946
WBC $10^{\wedge}9$/L, M (IQR)	4.17 (3.41~6.01)	5.03 (3.91~7.04)	-1.929	0.054
NEU $10^{\wedge}9$/L, M (IQR)	2.55 (1.86~4.03)	3.06 (2.17~4.49)	-1.388	0.165
LYM $10^{\wedge}9$/L, M (IQR)	1.23 (0.91~1.59)	1.23 (0.83~1.87)	-0.401	0.688
MON $10^{\wedge}9$/L, M (IQR)	0.35 (0.27~0.44)	0.35 (0.30~0.48)	-0.769	0.442
D-D mg/L, M (IQR)	0.35 (0.24~0.53)	0.27 (0.16~0.49)	-1.190	0.234

Note: In the table, M, IQR, *Z* indicate the same meanings as Table 2

Table 5: Comparison of abnormal rates of biochemical indexes between patients with basic diseases and patients without basic diseases [%(*n*/*N*)]

	The group with underlying disease	The group without of underlying disease	χ^2	*P*
TB %(*n*/*N*)	9.09 (5/55)	7.41 (4/54)	-	1.000
ALT % (*n*/*N*)	30.91 (17/55)	12.96 (7/54)	5.111[a]	0.024*
AST % (*n*/*N*)	23.64 (13/55)	7.41 (4/54)	5.452[a]	0.020*
ALP % (*n*/*N*)	4.44 (2/45)	12.24 (6/49)	-	0.271
γ-GT % (*n*/*N*)	20.00 (9/45)	8.16 (4/49)	2.758[a]	0.097

Note: In the table, %, *n*, *N*, χ^2,a,* indicate the same meanings as Table 1

Relationship between antiviral drug therapy and abnormal liver function in COVID-19 patients

Among the selected patients, 60 received one or more anti-SARS-CoV-2 drugs with data before treatment, 1 week after antiviral treatment (8^{th}–12^{th} day of treatment), and before discharge. Antiviral drugs include lopinavir/ritonavir tablets, recombinant human interferon α-2b spray, recombinant human interferon a-2b injections, abidor hydrochloride tablets, and ribavirin injections. As shown in Table 9, the two sets of data before and after antiviral treatment obeyed the abnormal distribution and underwent the Wilcoxon test. The TB, ALT, AST, and ALP levels were not statistically significant; the serum concentration of gamma-GT after 1 week of antiviral treatment was higher than before, and the difference was statistically significant ($P < 0.05$). As shown in Table 10, the two sets of biochemical indicators of antiviral treatment after 1 week and when discharged were tested. The abnormal rates of ALT and AST at discharge were significantly lower than those of antiviral treatment a week later. As shown in Table 11, the data of the two groups obeyed the abnormal distribution after 1 week of antiviral treatment and discharge, and they were tested in Wilcoxon's test. The ALT, ALP, and gamma-GT indicators were not statistically significant; the serum TB and AST concentrations of patients at discharge were lower than those before treatment, and the difference was statistically significant ($P < 0.05$).

Table 6: Median comparison of biochemical index concentration between patients with basic diseases and patients without basic diseases [M (IQR)]

	The group with underlying disease	The group without of underlying disease	*Z*	*P*
TB ummol/L, M (IQR)	10.86 (7.72~15.92)	8.72 (5.46~14.15)	-1.831	0.067
ALT U/L, M (IQR)	23.50 (16.00~43.25)	17.10 (12.60~26.10)	-2.645	0.008*
AST U/L, M (IQR)	28.15 (22.60~35.23)	22.50 (18.20~26.00)	-3.694	0.000*
ALP U/L, M (IQR)	59.00 (49.00~72.50)	56.50 (50.00~79.00)	-0.057	0.955
γ-GT U/L, M (IQR)	30.00 (19.00~46.78)	17.00 (12.25~30.50)	-2.959	0.003*

Note: In the table, M, IQR, Z,*indicate the same meanings as Table 2

Relationship between severity of COVID-19 patients and abnormal liver function of COVID-19 patients

According to the diagnostic criteria of the novel coronavirus Medical Treatment Plan (Seventh Edition), patients were divided into four categories: light, ordinary, severe, and critical, according to their clinical symptoms, physical examination, imaging examination, laboratory examination, digital pulse oxygen saturation, and oxygenation index. Because mild and common symptoms are similar and the disease is mild, severe, and critical cases have similar symptoms and serious illness, they were divided into two groups: mild/ordinary and severe/critical, with 95 cases (87.2%) in the mild/ordinary group and 14 cases (12.8%) in the severe/critical group. As shown in Table 12, the Chi-square test showed that TB, ALT, ALP, and γ-GT levels were not statistically significant. The abnormal rate of AST in the severe/critical type group was significantly higher than that in the mild/common type group. ($P < 0.05$) As shown in Table 13, the data of the two groups obey non-normal distribution, and the indexes of TB, ALT and ALP had no statistical significance by Mann–Whitney test, serum AST and γ-GT concentrations in severe/critical type group were significantly higher than those in mild/common type group ($P < 0.05$).

Discussion

The incidence of abnormal liver function in patients with COVID-19 varies among studies, and the incidence of abnormal liver function varies greatly from 4.8% to 78.0% in patients with COVID-19.[5] The main reason for this finding was the different evaluation criteria and statistical time points.[4,6] In this study, the incidence of abnormal liver function in patients with COVID-19 was 42.20%, the incidence of abnormal TB, ALT, AST, ALP and γ-GT were 8.26%, 22.0%, 15.60%, 8.5% and 13.8% respectively.

Table 7: Comparison of abnormal rates of biochemical indexes among patients with chronic liver disease, hypertension and diabetes mellitus [% (*n*/*N*)]

	Chronic liver disease	Hypertension	Diabetes	*P*
TB	0	21.05 (4/19)	10.00 (1/10)	0.105
ALT	42.11 (8/19)	36.84 (7/19)	30.00 (3/10)	0.812
AST	26.32 (5/19)	36.84 (7/19)	50.00 (5/10)	0.442
ALP	0	0	0	-
γ-GT	21.43 (3/14)	16.67 (3/18)	44.44 (4/9)	0.271

Note: In the table, %, *n*, *N*, χ^2 indicate the same meanings as Table 1

Literature reported that elderly patients are more likely to develop into severe or critical patients with COVID-19,[7] and meta-analysis shows that children and adolescents usually have a mild condition,[8] so theoretically, elderly patients with COVID-19 should have a higher risk of abnormal liver function. In this study, the incidence of liver function abnormalities appeared to be higher in COVID-19 patients aged <21 years.

In this study, it was found that the abnormal rates of ALT, AST and γ-GT in male patients were higher than those in female patients, which indicated that male patients with COVID-19 were more prone to liver cell damage and hepatobiliary cell damage. Research shows that there is gender escape in the expression of the *ACE2* gene, and the expression of ACE2 in the liver of women is obviously lower than that in men. The reason why the incidence of abnormal liver function in male patients with COVID-19 is higher than that in female patients may be related to the gender escape of ACE2 expression.[9] Another is maybe that the smoking rate of men is significantly higher than that of women, and smoking will lead to an increase in ACE2 gene expression, therefore ACE2 expression in men is higher than that in women.[10] The mechanism underlying abnormal liver function in patients with COVID-19 may be related to ACE2.[11] Therefore, men are more susceptible to SARS-CoV-2 and liver cells are more susceptible to SARA-CoV-2 from both of the above statements.

When the body is in a situation where infection, drugs, etc., can affect the immune function of the human body, it will produce an excessive immune response, and immune cells will release excessive inflammatory cytokines, resulting in the occurrence of "cytokine storm".[12,13] Because cytokines such as interleukin, tumor necrosis factor and interferon are not routine inspection items in clinical laboratories, C-reactive protein, CRP, as an inflammatory marker in the acute phase, can also reflect the degree of infection of the body well.[14] However, in this study, compared with COVID-19 patients with normal liver function and COVID-19 patients with abnormal liver function, there is no statistical difference in C-reactive protein, which may be related to the time point of detection.

D-dimer is a fibrin degradation product. When the human body is in a hypercoagulable state or fibrinolysis is hyperactive, the D-dimer levels increase. Many patients with COVID-19 often suffer from hypoxia in tissues and organs,[15] while the blood viscosity and serum D-dimer levels increase under hypoxia,

Table 8: Median comparison of biochemical index concentration of COVID-19 patients with chronic liver disease, hypertension and diabetes [M (IQR)]

	Chronic liver disease group	Hypertension group	Diabetes group	*Z*	*P*
TB umol/L, M (IQR)	11.73 (8.53~15.94)	11.51 (8.11~19.15)	12.32 (7.68~16.61)	0.174	0.917
ALT U/L, M (IQR)	26.00 (21.10~46.00)	24.00 (15.00~47.00)	26.40 (18.75~45.70)	1.061	0.588
AST U/L, M (IQR)	31.00 (24.00~41.00)	31.00 (26.00~52.00)	35.15 (29.75~53.00)	2.556	0.279
ALP U/L, M (IQR)	53.00 (45.75~62.00)	61.50 (52.00~75.50)	61.00 (50.0~78.5)	3.420	0.181
γ-GT U/L, M (IQR)	37.00 (23.25~50.75)	30.00 (15.00~44.75)	44.00 (26.50~94.00)	1.855	0.395

Note: In the table, M indicates the median, IQR indicates the interquartile spacing; Z indicates Wilcoxon test

therefore, this study researched the relationship between D-dimer and abnormal liver function in patients with COVID-19. However, this study found that D-dimer is not the reason for the increased risk of abnormal liver function.

The patients were divided into a basic disease group and a non-basic disease group. Among all liver biochemical indices, the abnormal rates of ALT and AST indices and median and interquartile distance in the basic disease group were significantly higher than those in the non-basic disease group, while TB, ALT and γ-GT had no significant significance, which indicated that patients with COVID-19 with the basic disease were more likely to have hepatocellular abnormalities mainly caused by elevated ALT and AST. Therefore, attention should be paid to the management of basic diseases.

When we investigated the relationship between antiviral treatment and abnormal liver function in patients with COVID-19, we found that the median concentration and interquartile range of serum γ-GT were significantly higher after one week of treatment than before treatment. Even if the values are within the normal range, we still cannot rule out the possibility of drug-induced liver injury. This study found that some patients did not find abnormal liver function before treatment, but appeared abnormal liver function after antiviral treatment, which may be related to the rate of disease progresses faster than that of drugs, so the body can have "cytokine storm" during this period, which leads to abnormal liver function; it may also be related to drug-induced liver injury during disease treatment, the antiviral drugs used to treat COVID-19, such as interferon-α, lopinavir/ritonavir and ribavirin,[5] have all reported liver injury.[16] To sum up, some patients in this study also have transient liver dysfunction during antiviral treatment, which also confirms that the serum γ-GT concentration of patients will increase after using antiviral drugs. Therefore, it is speculated that drug-induced liver injury may be the pathogenesis of abnormal liver function in COVID-19 patients.

In this study, compared with mild/common type and severe/critical type, the abnormal AST rate, median concentration and inter quartile distance of severe/critical type patients with COVID-19 were higher than those of mild/common type patients with COVID-19, which indicated that severe/critical type patients with COVID-19 were more likely to have liver function abnormality mainly caused by AST increase. The diagnostic criteria of severe/critical patients are all related to hypoxia, and ischemia and hypoxia of tissues and organs of patients with COVID-19 is a common pathophysiological phenomenon,[16-18] so we speculated that hepatic ischemia and hypoxia injury may be one of the pathogenesis of abnormal liver function in patients with COVID-19.

Table 9: Comparison of abnormal rates of biochemical indexes of patients after one week of antiviral treatment and at discharge [% (n/N)]

	Before antiviral treatment	After one week of antiviral treatment	χ^2	*P*
TB %(*n*/*N*)	8.33 (5/60)	6.67 (4/60)	-	1.000
ALT % (*n*/*N*)	25.0 (15/60)	33.33 (20/60)	1.008[a]	0.315
AST % (*n*/*N*)	16.67 (10/60)	15.00 (9/60)	0.063[a]	0.803
ALP % (*n*/*N*)	21.28 (1/47)	21.28 (1/47)	-	1.000
γ-GT % (*n*/*N*)	17.02 (8/47)	25.53 (12/47)	1.016[a]	0.313

Note: In the table, %, *n*, *N*, χ^2,a indicate the same meanings as Table 1

Conclusion

In conclusion, the incidence of abnormal liver function in patients with COVID-19 is 42.20%. Male sex, basic diseases, antiviral drugs, and severe or critical type are related to the occurrence of abnormal liver function in patients with COVID-19.

Ethical compliance

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional

Table 10: Median comparison of biochemical index concentrations of patients before and after antiviral treatment for one week(8-12days)[M(IQR)]

	Before antiviral treatment	After one week of antiviral treatment	*Z*	*P*
TB μmol/L, M (IQR)	9.95 (7.01~14.98)	10.00 (7.22~13.14)	-1.075[b]	0.282
ALT U/L, M (IQR)	22.75 (15.00~40.13)	29.00 (17.00~52.48)	-1.950[b]	0.051
AST U/L, M (IQR)	25.25 (20.00~34.50)	23.00 (17.40~36.75)	-0.585[b]	0.558
ALP U/L, M (IQR)	56.00 (49.00~72.00)	59.00 (45.00~68.00)	-1.017[b]	0.309
γ-GT U/L, M (IQR)	23.00 (15.00~37.00)	29.00 (18.00~48.00)	-2.112[b]	0.035*

Note: In the table, M, indicates the median, IQR indicates the interquartile spacing; b indicates positive rank; Z indicates Wilcoxon test

Table 11: Median comparison of biochemical index concentrations of patients after one week of antiviral treatment and at discharge [M (IQR)]

	After 1 week of antiviral treatment	On discharge	χ^2	*P*
TB % (*n*/*N*)	6.67 (4/60)	0	-	0.119
ALT % (*n*/*N*)	33.33 (20/60)	15.00 (9/60)	0.614[a]	0.019*
AST % (*n*/*N*)	15.00 (9/60)	3.33 (2/60)	4.904[a]	0.027*
ALP % (*n*/*N*)	21.28 (1/47)	21.28 (1/47)	-	1.000
γ-GT % (*n*/*N*)	25.53 (12/47)	23.40 (11/47)	0.594[a]	1.000

Note: In the table, %, *n*, *N*, χ^2,a,*indicate the same meanings as Table 1

Table 12: Comparison of abnormal rate of liver biochemical indexes between mild/ordinary patients and severe/critical patients [% (*n*/*N*)]

	Light/ordinary	Severe/critical	*P*
TB	9.37 (7/95)	14.29 (2/14)	0.325
ALT	22.11 (21/95)	21.43 (3/14)	1.000
AST	12.63 (12/95)	35.71 (5/14)	0.043*
ALP	8.54 (7/82)	8.33 (1/12)	1.000
γ-GT	13.41 (11/82)	16.67 (2/12)	0.670

Note: In the table 12, %, *n*, *N*, χ^2, *indicate the same meanings as Table 1

Table 13: Median comparison of liver biochemical index concentration between mild/common and severe/critical patients [M (IQR)]

	Light/ordinary type	Severe/critical type	*Z*	*P*
TB	9.50 (6.96~15.27)	10.41 (6.62~14.60)	-0.068	0.946
ALT	19.00 (13.00~38.00)	24.25 (18.75~33.10)	-1.237	0.216
AST	24.40 (20.00~29.00)	34.00 (24.00~50.20)	-2.478	0.013*
ALP	58.00 (50.00~75.00)	54.00 (39.75~84.25)	-0.850	0.395
γ-GT	20.00 (13.75~36.25)	31.00 (23.00~49.93)	-2.012	0.044*

Note: In the table, M, IQR, *Z*, *indicate the same meanings as Table 2

and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflicts of interest

There are no conflicts of interest.

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