

Original

Effects of the COVID-19 Pandemic on Patients with Alcoholic Liver Disease

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Summary

Background: The coronavirus disease 2019 (COVID-19) pandemic has caused many people mental distress. Negative changes have been reported in physical activity, sleep, alcohol consumption, and smoking. Many patients with alcoholic liver disease (ALD) have a tendency for alcohol dependence, but there are no reports on how the COVID-19 pandemic has affected ALD patients.

Aims: The purpose of this study was to clarify the effects of the COVID-19 pandemic on ALD patients.

Methods: The study consisted of two parts. In the first part, changes in the alcohol consumption and blood biochemistry of ALD patients who continued to visit our hospital as outpatients before and during the COVID-19 pandemic were compared. In the second part, the clinical backgrounds at the time of the initial examination of ALD patients who were first examined in the year before the COVID-19 pandemic (before outbreak group) and ALD patients who were first examined in the six months after the start of the COVID-19 pandemic (after outbreak group) were compared. Patients in the after outbreak group were asked whether their motivation to drink was related to the COVID-19 pandemic.

Results: In part 1, of the 95 ALD patients surveyed, alcohol consumption increased after the start of the pandemic in 20 (21.1%) patients, and 13 (65%) of these 20 patients blamed the increase on the COVID-19 pandemic. Gamma-glutamyltransferase levels increased and prothrombin activity (PT%) decreased markedly after the start of the pandemic in the 20 patients in this increased alcohol consumption group. Although 32 patients reported that their alcohol consumption remained unchanged, liver function appeared to deteriorate after the start of the pandemic, which suggests that ALD patients' self-reports of alcohol consumption were inaccurate. In part 2, the clinical backgrounds of 28 ALD patients first examined in our hospital in the year before the COVID-19 pandemic and 12 ALD patients first examined in the six months after the start of the pandemic were compared. Liver damage was more severe in the after outbreak group, and 8 of these 12 patients (66.7%) blamed their drinking on the COVID-19 pandemic. Although the difference was not significant, there tended to be more employed people among the ALD patients who were first examined after the start of the COVID-19 pandemic.

Conclusion: Liver function in ALD worsened due to the COVID-19 pandemic. In some ALD patients who were first examined for ALD after the start of the pandemic, the motive for drinking was associated with the COVID-19 pandemic.

Key Words: Alcohol dependence, Alcoholic liver disease, COVID-19, COVID-19 pandemic, Declared states of emergency

Introduction

Coronavirus disease 2019 (COVID-19) started in the city of Wuhan, China, in December 2019 and spread rapidly throughout the world. It was declared a global pandemic by the World Health Organization on March 11, 2020. In Japan, the first infected person was con-

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firmed on January 15, 2020, and in February, a outbreak occurred on the Diamond Princess, a cruise ship anchored at Yokohama. That same month, Japan's first outbreak was confirmed in Hokkaido¹⁾. By April 29, 2020, there were a total of 13852 cases and 389 deaths in Japan²⁾.

To prevent the spread of infection, avoidance of the three Cs (closed spaces, crowded places, close-contact settings) and behaviors to maintain social distancing were recommended. Then, on April 7, 2020, Japan's Prime Minister declared states of emergency in Tokyo, Kanagawa, Saitama, Chiba, Osaka, Hyogo, and Fukuoka prefectures. On April 16, 2020, he extended the state of emergency to the entire nation.

These self-restraint behaviors and staying at home, together with the fear of the COVID-19 pandemic, caused many people mental distress. Stanton et al. reported negative changes in physical activity in 48.9% of people, in sleep in 40.7%, in alcohol consumption in 26.6%, and in smoking in 6.9%³⁾. Many patients with alcoholic liver disease (ALD) have a tendency for alcohol dependence, but there are no reports on how the COVID-19 pandemic has affected ALD patients. The purpose of this study was to clarify the effects of the COVID-19 pandemic on ALD patients.

Methods

The diagnosis of ALD was made in accordance with the diagnostic criteria (2011) of the Japanese Society for Biomedical Research on Alcohol. These criteria are ethanol intake of ≥ 60 g/day in men, ≥ 40 g/day in women, history of alcohol intake of ≥ 5 years, and liver damage in people negative for hepatitis virus markers. Patients with autoimmune hepatitis, hepatocellular carcinoma or other cancer were excluded.

The following investigations were done, with the period up to February 2020 taken as before the COVID-19 pandemic and from March 2020 onward as during the COVID-19 pandemic. This study was reviewed and approved by the Ethics Committee of the Dokkyo Medical University Saitama Medical Center. It was a retrospective, observational study conducted after posting information about the study on the hospital's website.

Investigation 1: The subjects were ALD patients who continued to visit the hospital as outpatients be-

fore and during the COVID-19 pandemic. Changes in their alcohol consumption, blood biochemistry (AST (aspartate transaminase), ALT (alanine aminotransferase), LDH (lactate dehydrogenase), GGT (γ -glutamyltransferase), total bilirubin, albumin), and white blood cells, hemoglobin, platelets, and prothrombin activity (PT%) from before to during the pandemic were compared.

Alcohol consumption status before and during the COVID-19 pandemic was confirmed based on medical records. Subjects were divided into three groups depending on changes in their alcohol consumption: a group that continued to abstain from alcohol, a group with the same alcohol consumption as before the pandemic, and a group with increased alcohol consumption. The trends in GGT and PT% in these three groups were compared. The group with increased alcohol consumption was asked whether their motivation to drink had been affected by the COVID-19 pandemic.

The occupations of the people in the three above-mentioned groups prior to the COVID-19 pandemic were also investigated. Their occupations were classified into seven categories: management, clerical work, technical work, manufacturing/construction/transportation, service industry, unemployed, and unknown.

Investigation 2: The clinical background characteristics at the time of the initial examination of ALD patients who were first examined in the year before the COVID-19 pandemic (March 2019 to February 2020) (before outbreak group) and ALD patients who were first examined in the six months after the start of the COVID-19 pandemic (March to August 2020) (after outbreak group) were compared. Patients in the after outbreak group were asked whether their motivation to drink was related to the COVID-19 pandemic. Their occupations at the time of the initial examination were also investigated. The occupational categories were the same as in Investigation 1.

Blood biochemistry test values are shown as means \pm standard deviation. The statistical analysis of data from before and during the COVID-19 pandemic was done using the Wilcoxon test and chi-squared test, with $P < 0.05$ taken to indicate a significant difference.

Results

Investigation 1: Ninety-five ALD patients were con-

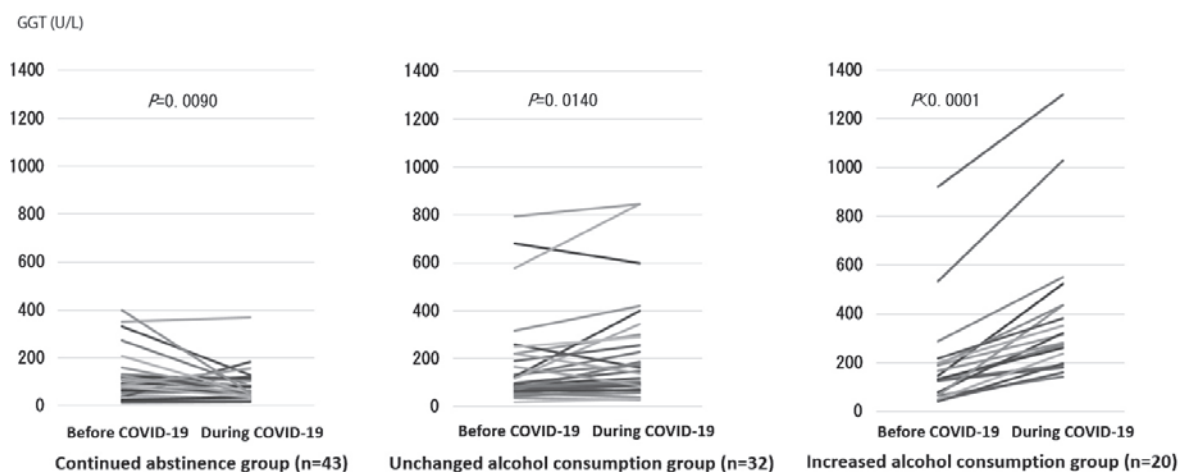


Figure 1 Changes in GGT by alcohol consumption status

In the continued abstinence group ($n = 43$), GGT is 82.4 ± 21.6 U/L before the COVID-19 pandemic and 67.1 ± 26.5 U/L after the start of the pandemic, a significant decrease ($P = 0.0136$). In the increased alcohol consumption group ($n = 20$), GGT is 191.6 ± 203.7 U/L before the pandemic and 390.9 ± 291.5 U/L after the start of the pandemic, whereas in the unchanged alcohol consumption group ($n = 32$), it is 181.1 ± 191.2 U/L before the pandemic and 217.1 ± 211.5 U/L after the start of the pandemic. Both are significant increases ($P = 0.0005$, $P = 0.0140$).

Table 1 Changes in the clinical parameters from before to during the COVID-19 pandemic ($n = 95$)

	Before pandemic	During pandemic	<i>P</i> value
AST (U/L)	41.5 ± 27.6 (12-153)	220.6 ± 1185.8 (18-10991)	0.0002
ALT (U/L)	30.2 ± 22.1 (10-52)	116.6 ± 656.2 (11-60)	0.0002
LDH (U/L)	202.9 ± 56.1 (120-545)	280.2 ± 396.4 (119-2945)	0.0009
GGT (U/L)	142.1 ± 162.9 (13-920)	184.9 ± 222.7 (14-1299)	0.0013
T-Bil (mg/dL)	1.2 ± 0.8 (0.3-5.3)	1.6 ± 1.7 (0.3-12.0)	0.0011
Alb (g/dL)	3.9 ± 0.6 (2.3-5.0)	3.9 ± 0.6 (2.1-5.1)	0.3402
WBC ($10^3/\mu\text{L}$)	5.8 ± 2.0 (2.5-12.5)	6.0 ± 2.0 (2.8-14.5)	0.1806
Hb (g/dL)	13.1 ± 2.54 (7.4-17.5)	13.3 ± 2.2 (7.2-17.8)	0.1203
Plt ($10^4/\mu\text{L}$)	17.1 ± 8.2 (3.2-44.29)	15.8 ± 7.7 (2.7-41.1)	0.0016
PT% (%)	84.4 ± 23.9 (31.1-150.1)	76.6 ± 25.9 (5.4-134.9)	0.0033

AST, aspartate transaminase; ALT, alanine aminotransferase;

LDH, lactate dehydrogenase; GGT, γ -glutamyltransferase; T-Bil, total bilirubin;

Alb, albumin; WBC, white blood cells; Hb, hemoglobin; Plt, platelets;

PT%, prothrombin activity

firmed to have visited the hospital both before and during the COVID-19 pandemic. Their mean age was 57.6 years (30-87 years), 73 were male, and 22 were female. With regard to changes in their alcohol consumption from before to during the pandemic, 43 patients continued to abstain, 32 patients consumed the same amount as before, and 20 patients had increased consumption. In the increased consumption group, 13 patients responded that COVID-19 had affected their drinking, and 7 responded that it had not.

During the observation period, five patients required hospitalization, two required emergency endoscopic procedures due to hematemesis, and two died after hospitalization. All of these cases were triggered by increasing alcohol add consumption due to the COVID-19 pandemic.

The trends in blood biochemistry test results for the 95 patients before and during the COVID-19 pandemic are shown in Table 1. Significant increases were seen in AST, ALT, LDH, and GGT after the start of the

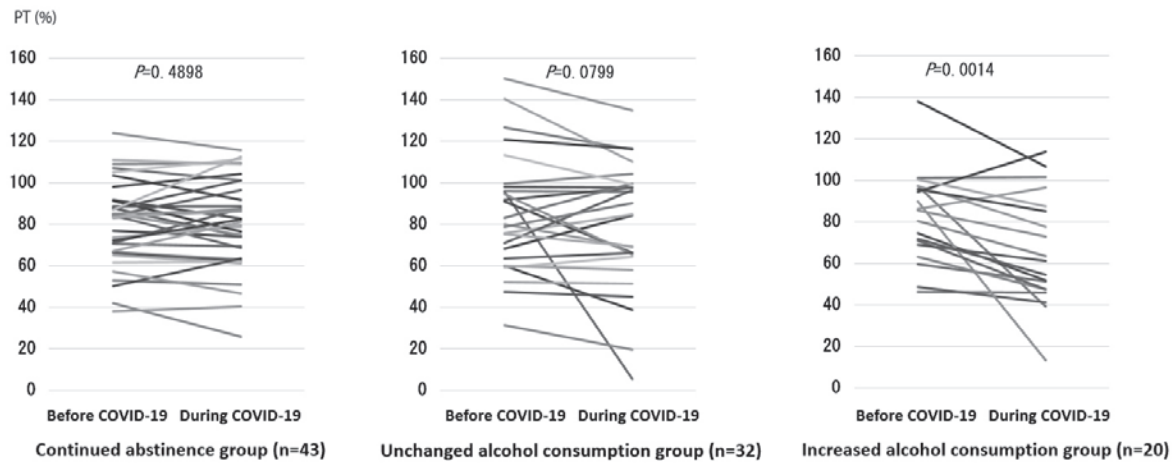


Figure 2 Changes in PT% by alcohol consumption status

In the continued abstinence group (n = 43), PT% is 82.6% ± 21.2% before the COVID-19 pandemic and 80.0% ± 21.4% after the start of the pandemic, not a significant difference (P = 0.4898). In the unchanged alcohol consumption group (n = 32), it is 87.8% ± 27.7% before the pandemic and 79.1% ± 29.6% after the start of the pandemic. Although it decreases after the start of the pandemic, the difference is not significant (P = 0.0799). In the increased alcohol consumption group (n = 20), PT% is 82.5% ± 21.6% before the pandemic and 67.0% ± 26.5% after the start of the pandemic, a significant decrease (P = 0.0013).

pandemic compared with before the pandemic. Significant decreases were seen in platelet counts and PT%. No significant changes were seen in total bilirubin, albumin, white blood cell count, hemoglobin, or platelet count.

The changes in GGT for each alcohol consumption group are shown in Fig. 1. In the continued abstinence group (n = 43), GGT was 82.4 ± 21.6 U/L before the COVID-19 pandemic and 67.1 ± 26.5 U/L after the start of the pandemic. A significant improvement was observed (P = 0.0090). In the increased alcohol consumption group (n = 20), GGT was 191.6 ± 203.7 U/L before the COVID-19 pandemic and 390.9 ± 291.5 U/L after the start of the pandemic, a significant increase (P < 0.0001). In the group whose alcohol consumption remained the same (n = 32), GGT was 181.1 ± 191.2 U/L before the COVID-19 pandemic and 217.1 ± 211.5 U/L after the start of the pandemic. A significant elevation was observed even in this group (P = 0.0140).

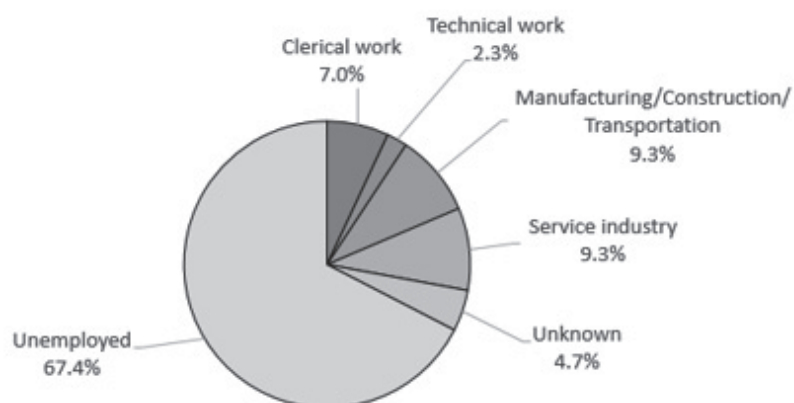
The changes in PT% for each alcohol consumption group are shown in Fig. 2. In the continued abstinence group, PT% was 82.6% ± 21.2% before the COVID-19 pandemic and 80.0% ± 21.4% after the start of the pandemic; there was no significant difference (P = 0.4898). In the group whose alcohol consumption remained the same (n = 32), PT% was 87.8% ± 27.7% before the COVID-19 pandemic and 79.1% ± 29.6% after

the start of the pandemic; although it decreased after the start of the pandemic, the difference was not significant (P = 0.0799). In the increased alcohol consumption group (n = 20), PT% was 82.5% ± 21.6% before the COVID-19 pandemic and 67.0% ± 26.5% after the start of the pandemic, a significant decrease (P = 0.0013).

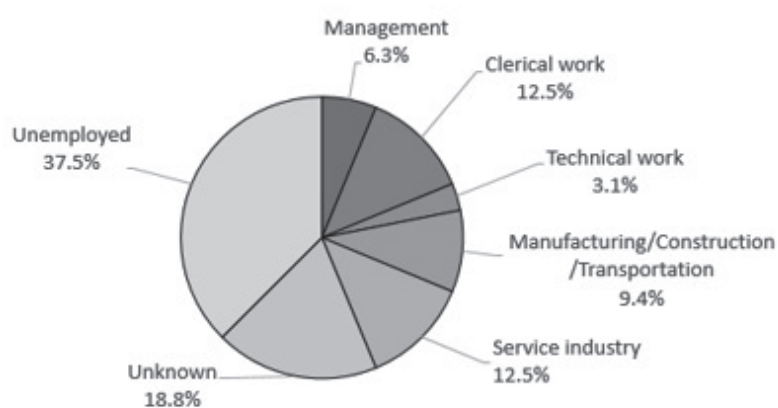
Fig. 3 shows the occupation distribution by the change in the amount of alcohol consumed. No difference was seen in the occupation distributions in the group whose alcohol consumption remained the same and in the increased alcohol consumption group. In the continued abstinence group, 29 of the 43 people (67.4%) were unemployed, significantly higher than the 12 of 32 (37.5%) in the group whose alcohol consumption remained the same and the 8 of 20 (40.0%) in the increased alcohol consumption group (P = 0.0192, P = 0.0395).

Investigation 2: Twenty-eight ALD patients were first examined in the year before the COVID-19 pandemic, and 12 ALD patients were first examined in the 6 months after the start of the COVID-19 pandemic. Of the after outbreak group eight patients responded that the COVID-19 pandemic had affected their motivation to drink, and 2 patients responded that it had not. The remaining 2 patients did not respond.

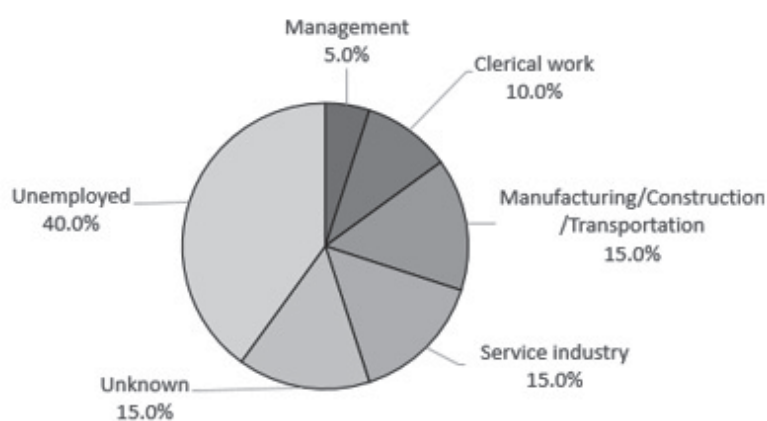
Table 2 shows the clinical characteristics of the ALD



Continued abstinence group (n=43)



Unchanged alcohol consumption group (n=32)



Increased alcohol consumption group (n=20)

Figure 3 Occupation distribution by alcohol consumption status

In the continued abstinence group, 29 of the 43 people (67.4%) are unemployed, significantly higher than the 12 of 32 (37.5%) in the group whose alcohol consumption remains the same and the 8 of 20 (40.0%) in the increased alcohol consumption group ($p = 0.0192$, $p = 0.0395$). No significant difference is seen in the occupation distribution of the three groups in those who are employed.

Table 2 Clinical characteristics in the before outbreak group and after outbreak group at initial diagnosis

	Before outbreak group (n = 28)	After outbreak group (n = 12)	P value
Age (y)	57.7 ± 12.7	56.2 ± 9.2	0.7452
Sex (male/female)	19/9	10/9	0.4544
AST (U/L)	104.9 ± 141.5	1035.3 ± 3135.8	0.0098
ALT (U/L)	44.6 ± 43.8	596.2 ± 1828.3	0.0030
LDH (U/L)	266.1 ± 124.3	698.1 ± 1011.5	0.1400
GGT (U/L)	308.4 ± 310.0	479.5 ± 409.1	0.1480
T-Bil (mg/dL)	1.97 ± 1.88	5.76 ± 6.25	0.0213
Alb (g/dL)	3.48 ± 0.74	3.15 ± 0.83	0.2497
WBC (10 ³ /μL)	7275.0 ± 3636.1	7941.7 ± 2974.0	0.2619
Hb (g/dL)	11.8 ± 2.7	11.3 ± 3.1	0.5451
Plt (10 ⁴ /μL)	17.3 ± 8.2	11.1 ± 7.2	0.0231
PT% (%)	82.0 ± 27.0	62.2 ± 30.4	0.0897

AST, aspartate transaminase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; GGT, γ -glutamyltransferase; T-Bil, total Bilirubin; Alb, albumin; WBC, white blood cells; Hb, hemoglobin; Plt, platelets; PT%, prothrombin activity

patients who were first examined before the COVID-19 pandemic and those who were first examined after the start of the pandemic. No significant differences were seen between these two groups in age or male-female ratio.

AST at the time of the initial examination was 104.9 ± 141.5 U/L in the before outbreak group and 1035 ± 3135.8 U/L in the after outbreak group. The level was significantly higher in the after outbreak group ($P = 0.0098$). Similarly, ALT was 44.6 ± 43.8 U/L in the before outbreak group and 596.2 ± 1828.3 U/L in the after outbreak group, whereas total bilirubin was 1.97 ± 1.88 mg/dL in the before outbreak group and 5.76 ± 6.25 mg/dL in the after outbreak group. Both were significantly higher in the after outbreak group ($P = 0.0030$, $P = 0.0213$). GGT tended to be higher in the after outbreak group, but no significant difference was seen ($P = 0.1480$).

The platelet count was 17.3 ± 8.2 × 10⁴/mm³ in the before outbreak group and 11.1 ± 7.2 × 10⁴/mm³ in the after outbreak group, significantly lower in the after outbreak group ($P = 0.231$). PT% tended to be lower in the after outbreak group, but no significant difference was seen ($P = 0.0900$).

Occupations in the before outbreak group and the after outbreak group are shown in Fig. 4. Fifteen of 28 (53.6%) people in the before outbreak group were unemployed. This was higher than the 4 of 12 (33.3%) in the after outbreak group, but the difference was not

significant ($P = 0.2402$).

Discussion

In Western countries, it has been reported that alcohol consumption decreased after the start of the COVID-19 pandemic compared with before the pandemic⁴. The reasons are assumed to be that restaurants and bars that serve alcohol were temporarily closed, and that alcohol sales were regulated in some areas³. A survey of 2307 people by Callinan et al., however, found that there had been no change in daily alcohol consumption overall before and during the pandemic. They also demonstrated that, whereas alcohol consumption decreased in young men and people who usually drank only at home, alcohol consumption increased in people with high levels of stress⁵.

Voluntary behavioral restrictions to prevent the spread of infections are a cause of mental stress, and about half of people are reported to have had moderate to severe psychological effects⁶. Exposure to stress is reported to increase the risk of alcohol use disorders⁷, and it is conjectured that alcohol consumption may readily increase in ALD patients as a result of stress.

In investigation 1 in the present study, 95 ALD patients who continued outpatient visits to our hospital before and during the COVID-19 pandemic were surveyed. Alcohol consumption increased after the start of the pandemic in 20 (21.1%) of the 95 patients. Thir-

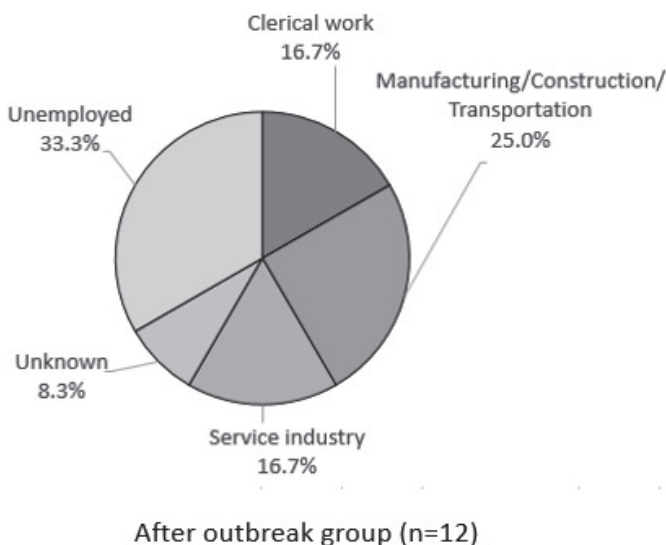
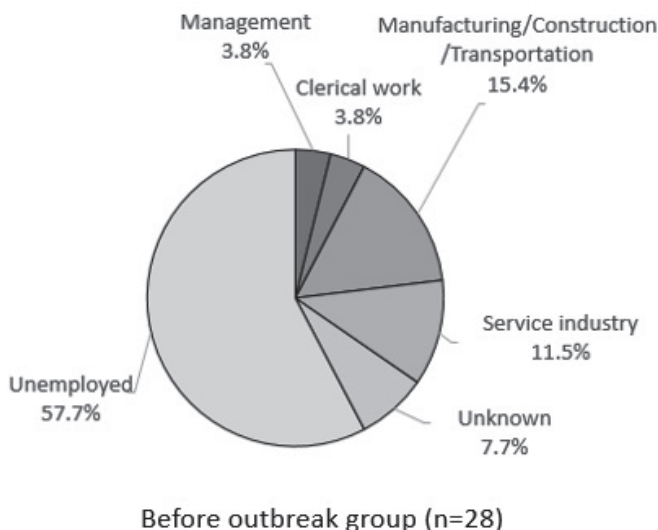


Figure 4 Occupation distribution in the before outbreak group and after outbreak group at initial diagnosis. Fifteen of 28 (53.6%) people in the before outbreak group are unemployed. This tends to be higher than the 4 of 12 (33.3%) in the after outbreak group, but the difference is not significant ($p = 0.2402$). No significant difference is seen in the occupation distribution of the two groups in those who are employed.

teen (65%) of these 20 patients responded that the cause of the increase was the COVID-19 pandemic. GGT increased and PT% decreased markedly after the start of the pandemic in the 20 patients in this increased alcohol consumption group, which is thought to be the reason for the worsening data for the 95 patients overall.

Even in the 32 patients whose alcohol consumption was the same as before the pandemic, GGT increased significantly, and PT% tended to decline after the start

of the pandemic. This result is thought to show the inaccuracy of ALD patients' self-reports of alcohol consumption.

The results of the investigation of occupation by amount of alcohol consumption showed that there were more unemployed patients in the continued abstinence group than in the other two groups. This could be because the COVID-19 pandemic made it more difficult for employed ALD patients to abstain. Thus, temporary unemployment and reduced income due to the

COVID-19 pandemic may be factors related to motivation for increase or decrease in drinking.

In investigation 2, the clinical backgrounds at the time of the initial examination of 28 ALD patients who were first examined in our hospital in the year before the COVID-19 pandemic and 12 ALD patients who were first examined in the six months after the start of the pandemic were compared. No differences were seen in age or sex between the two groups, but the liver damage was more severe for the initial examination in the after outbreak group. Of the 12 patients in the after outbreak group, the motivation for drinking was related to the COVID-19 pandemic in 8 patients (66.7%).

The investigation of occupation at the time of the initial examination showed that, of the ALD patients who were first examined in the year before the COVID-19 pandemic, 53.6% were unemployed, whereas of the ALD patients who were first examined after the start of the pandemic, 33.3% were unemployed. Although the difference was not significant, there tended to be more employed people among the ALD patients who were first examined after the start of the COVID-19 pandemic. This suggests the possibility that the COVID-19 pandemic had a stronger effect on mental stress of employed ALD patients.

In a survey of 1982 people, Weerakoon et al. found that 34% consumed large amounts of alcohol during the COVID-19 pandemic⁸. This is thought to coincide with the results of the present study. The COVID-19 pandemic led to an economic recession, which increased the number of unemployed people. There is a concern about an increase in suicides due to fear of infection and financial stress, including unemployment^{9,11}. Also, in the present study, unemployment and reduced income due to the pandemic were conjectured to be a motivation for drinking.

There are several reports about COVID-19 and chronic liver damage. It has been reported that 3% of infected people have chronic liver damage¹², and worsening liver damage was seen in about 13-53% of patients during treatment for COVID-19¹³. Worsening liver damage is often seen during treatment of patients with chronic liver damage, particularly nonalcoholic fatty liver disease patients^{14,15}. In cirrhosis patients, the mortality rate from COVID-19 increases in

those with lower hepatic reserve¹⁶. Although the number of reported cases is small, it is also known that ALD patients have more serious condition during COVID-19 infections^{17,18}. However, there have been no reports of how liver damage in ALD patients has been affected by the COVID-19 pandemic. Although it is necessary to take into account the strong restraint and suppression of medical visits after the COVID-19 pandemic, this is the first report showing that liver damage in ALD patients has been exacerbated by the COVID-19 pandemic.

Conclusions

Liver function in ALD outpatients worsened due to the COVID-19 pandemic. Alcohol consumption increased in 21.1% of ALD patients during the pandemic. The liver function of ALD patients who were first examined after the start of the pandemic was worse than that of patients who were first examined before the pandemic. The motivation for drinking alcohol was related to the COVID-19 pandemic in 66.7% of ALD patients who were first examined for ALD after the start of the pandemic.

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