

## Hazardous environmental factors enhance impairment of liver function in HBV and HCV hepatitis

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## 1. ABSTRACT

Hepatitis B virus (HBV) and hepatitis C virus (HCV) often cause chronic liver disease. We hypothesized that environmental factors adversely impact the liver function in workers with these types of hepatitis. We used liver function tests including aspartate aminotransferase, alanine aminotransferase, and  $\gamma$ -glutamyltransferase to evaluate whether hazardous work conditions increase the incidence of chronic liver disease among HBV and HCV infected workers. Organic solvent, night work, visual display terminals, dust, lead, vibrations, and ionizing radiation all led to increased impairment of liver function in patients with hepatitis as compared to the control group that were not exposed to such agents. Therefore, hazardous working conditions have to be carefully considered in the progress of chronic liver disease in workers infected with HBV and HCV.

## 2. INTRODUCTION

In Japan, over one million individuals are infected by HBV and over two million individuals are infected by HCV (<http://www.med.or.jp/kansen/>). HBV and HCV are the major cause of chronic liver disease including cirrhosis and hepatocellular carcinoma (1-2). In Japan, some workers are engaged in hazardous works (HW). The hazardous work is defined by Paragraph 2 of Article 13 in the Ordinance on Industrial Safety and Health (The Ministry Of Labour Ordinance No32, September 30, 1972) ([http://www.jniosh.go.jp/icpro/jicosh-old/japanese/country/japan/laws/03\\_rel/01\\_safetyandhealth\\_reg/vol01/02/e.html](http://www.jniosh.go.jp/icpro/jicosh-old/japanese/country/japan/laws/03_rel/01_safetyandhealth_reg/vol01/02/e.html)). Solvent mixtures (3), vinyl chloride (4-6), and dimethylformamide, which are reported among such hazards, are known to target the liver (7-9). In Japan, over 1,700,000 individuals are engaged in HW and are required to have medical examination under the laws of occupational health.

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Since HBV and HCV do not cause subjective symptoms, many patients with HBV and HCV hepatitis are unknowingly involved in HW. There are few follow up surveys as how the liver function of patients with HBV and HCV might be affected by HW. Preclinical assays of liver function include determining the serum activity of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and  $\gamma$ -glutamyltransferase (GGT), alkaline phosphatase and serum level of total bilirubin, bile acids, and/or sorbitol dehydrogenase activity. Increase in serum AST activity is due to damage or injury to liver, heart or skeletal muscle. Due to infrequent false negative and limited false positive results, serum ALT activity level is considered as the gold standard clinical marker of liver injury. Despite this, serum ALT activity is also increase in cases of muscle necrosis. Serum AST activity is considered a less specific biomarker of liver injury as compared to ALT activity. The ratio of serum AST to ALT can be used to differentiate liver damage from other organ injuries. Serum ALT level is greater than AST level in certain types of chronic liver disease such as hepatitis. GGT activity is localized to liver, kidney, and pancreatic tissues. In humans, GGT activity is used as a marker of hepatobiliary injury, especially cholestasis and biliary stasis, and bears a high sensitivity and a low false negative rate (10). Serum aminotransferases (or transaminases) are indicators for evaluation of liver function and are increased upon alcohol consumption (11-13), body mass index (BMI) (14-15), viral hepatitis, and by occupational hepatotoxicity. Nevertheless, in up to one third of patients with HCV infection the serum aminotransferase level remains normal (16).

We hypothesized that environmental factors adversely impact the liver function in workers with these types of hepatitis. To this end, we investigated the effects of HW on the workers infected with HBV and HCV using data collected over a span of 5 years. We compared the serum AST, ALT, and GGT activities in patients with HBV and HCV infected workers who were engaged in HW. Patients who were not subjected to such hazardous conditions (usual work or UW) were used as controls.

### 3. MATERIALS AND METHODS

#### 3.1. Definition of terms concerning occupational health

##### 3.1.1. Hepatitis workers

In this study, we included patients who were infected with HBV and HCV, were carriers, or had chronic hepatitis, hepatic cirrhosis, or hepatic cancer.

##### 3.1.2. Hazardous works

In this study, hazardous works were due to organic solvents, night work, visual display terminals (VDT), dust, lead, vibrations, or ionizing radiation.

##### 3.1.3. Usual work

In this study, usual work was considered a work that was not requiring a medical examination according to the above Ordinance.

#### 3.2. Objects and questionnaires

Included in this study were workers who had

checkup medical examination as well as required laboratory data at a hospital. This included 183,463 Japanese with assessed serum aminotransferases and 19549 workers (1815 factories) who were engaged in HW. Among the 183,463 patients, we selected 124 patients with hepatitis. For establishment of a control group, we first randomly selected 366 healthy individuals who were co-workers of patients with hepatitis. After being matched for age, sex, smoking habits, alcohol consumption, exercising habits, and body mass, we selected 248 controls. All surveys were carried out after obtaining the permission of the ethics committee of the University of Occupational and Environmental Health, Japan. For each patient, smoking history, alcohol consumption, and exercising habits were obtained. Subjects were defined as 'drinkers' if they drank over 20 gram ethanol per day. Smokers were defined as those who smoked over one cigarette per day. Regular exercise was considered only if was performed each day.

We carried out the following analysis in the case-control study

1<sup>st</sup> step: Comparison of workers with hepatitis with controls  
2<sup>nd</sup> step: Comparison of workers with hepatitis engaged in HW with workers with hepatitis engaged in UW  
3<sup>rd</sup> step: Comparison among the four groups (Figure 1)

#### 3.3. Examinations

Activity of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and  $\gamma$ -glutamyltransferase (GGT) was measured using a JCA-BM2250 autoanalyser (Japan Electron Optics Laboratory Co.Ltd., Japan). The height and weight of all workers were measured each year and body mass index was calculated according to the formula (weight in Kilogram)/(height in meter)<sup>2</sup>. Abnormal results for the serum AST, ALT, and GGT levels defined as AST>40 (IU/L), ALT>35 (IU/L), or GGT>70 (IU/L). Data about life style (smoking habits, alcohol consumption, and exercising habits) were collected by a self-administered questionnaire each year.

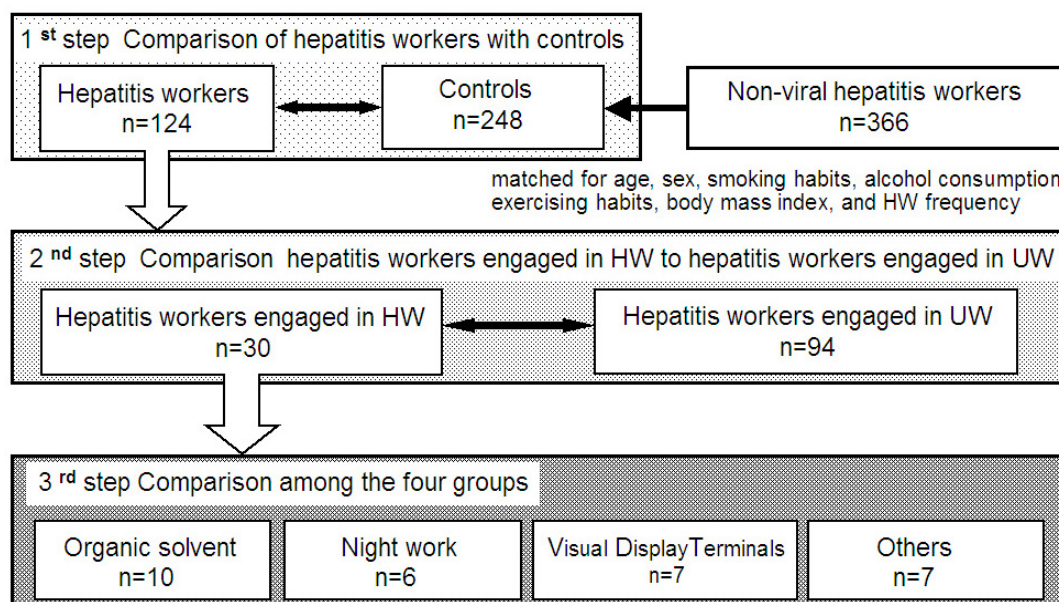
#### 3.4. Statistics

Data concerning mean age, body mass index, and AST, ALT, and GGT are expressed as mean $\pm$ S.D. In the analysis of characteristics, continuous variables were compared using unpaired t-tests, and categorical variables were compared using the chi-squared test. Two way repeated measures ANOVA was used for determination of significant differences between the 4 groups of HW. In all cases, significance was determined by a *P* value<0.05. Analyses were performed using StatView5.0 for windows, SAS Institute, Inc., Cary, NC, USA.

### 4. RESULTS

#### 4.1. 1<sup>st</sup> step: Comparison of workers with hepatitis with controls

As shown in Table 1, the parameters in life history did not show any significant difference between workers with hepatitis and controls. Mean serum levels of AST and ALT in workers with hepatitis were significantly higher than those in the controls (Table 2). However, there was no



**Figure 1.** Flow chart giving an outline of this study. In the 1st step, we compared workers with hepatitis with controls. In the 2nd step we took workers with hepatitis as the subjects, and compared workers with hepatitis engaged in hazardous works (HW) to workers with hepatitis engaged in usual works (UW). In the 3rd step we took workers with hepatitis engaged in HW as subjects, and compared four groups (organic solvent; night work; visual display terminals; and others including dust, lead, vibrations, and ionizing radiation) categorized by kinds of hazardous works.

significant difference in mean serum GGT levels between workers with hepatitis and the controls (Table 2). The frequencies of abnormalities in the serum level of AST and ALT levels in workers with hepatitis were significantly higher than those in the controls (Table 3). However, there were no significant differences in the frequencies of abnormalities in the GGT level between workers with hepatitis and controls (Table 3).

#### 4.2. 2<sup>nd</sup> step: Comparison of workers with hepatitis engaged in hazardous works (HW) with workers with hepatitis engaged in usual works (UW)

When factors such as sex, smoking, alcohol, exercise, and body mass index were considered, there was no significant difference between workers with hepatitis engaged in HW and workers with hepatitis engaged in UW although the mean age of workers with hepatitis engaged in UW was significantly higher than that of workers with hepatitis engaged in HW (Table 4). Mean serum level of AST and ALT in workers with hepatitis engaged in HW was significantly higher than those in workers with hepatitis engaged in UW (Table 5). But there were no significant differences in mean GGT between workers with hepatitis engaged in HW and workers with hepatitis engaged in UW (Table 5).

The frequency of abnormalities in serum level of AST and ALT in workers with hepatitis engaged in HW were significantly higher than those in workers with hepatitis engaged in UW (Table 6). Nevertheless, there were no significant differences in the frequencies of abnormalities in the GGT level between workers with hepatitis engaged in HW and workers with hepatitis engaged in UW (Table 6).

#### 4.3. 3<sup>rd</sup> step: Comparison among the four groups

There were no significant differences among the four groups with respect to the mean age, sex, smoking, alcohol, exercise, and body mass index (Table 7). Table 8 and Figure 2 show serum AST, ALT, and GGT levels of the four groups (workers with hepatitis exposed to organic solvents (OS), night works, VDT, dust, lead, vibrations, and ionizing radiation). AST, ALT, and GGT were not significantly different among the four groups. However, serum level of AST, ALT, and GGT of workers with hepatitis involved with OS seemed to be higher than those in workers with hepatitis involved with night work, VDT, or the others. Therefore, workers with hepatitis with HW were divided into two categories: workers with hepatitis exposed to organic solvents (OS) and those exposed to the 'others' (including night work, VDT, dust, lead, vibrations, and ionizing radiation) (OT). Table 9 shows AST, ALT, and GGT OS workers with hepatitis and OT hepatitis workers. Mean serum AST, ALT and GGT in OS workers with hepatitis were significantly higher than those in OT hepatitis workers. Table 10 shows the frequency of abnormalities in AST, ALT, and GGT. The frequencies of abnormalities in GGT in workers with hepatitis involved with OS were significantly higher than those in workers with hepatitis with involved the OT.

## 5. DISCUSSION

Throughout the course of the study, the activity of serum aminotransferase in workers with hepatitis who were engaged in HW were almost always higher than those in the control group. This suggests that HW enhances the impact of

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**Table 1.** Parameters in life history of workers with hepatitis and controls

		Hepatitis workers	Controls	p
Number		124	248	
Mean age		47.1±8.2	45.5±8.9	0.10
Sex	Male	105	196	0.19
	Female	19	52	
Smoking	Smoker	52	107	0.90
	Non smoker	72	141	
Alcohol	> 20g/day	43	98	0.36
	< 20g/day	81	150	
Exercise	Yes	59	115	0.29
	No	65	133	
BMI		23.3±2.9	23.2±3.0	0.60
HW	Yes	30	42	0.09
	No	94	206	

Data are expressed as mean±S.D. BMI, body mass index; HW, hazardous works. Not significantly different compared to each parameter

**Table 2.** A comparison of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and  $\gamma$ -glutamyltransferase (GGT) levels in workers with hepatitis with controls

	Mean AST		Mean ALT		Mean GGT	
Year	Hepatitis workers	Controls	Hepatitis workers	Controls	Hepatitis workers	Controls
1	35.6±28.1 <sup>1</sup>	22.9±9.7	47.7±69.1 <sup>1</sup>	28.3±19.8	56.5±66.5	44.2±54.6
2	37.1±28.8 <sup>1</sup>	23.4±13.7	48.6±54.2 <sup>1</sup>	29.8±23.8	59.7±68.6	49.9±51.4
3	36.8±28.9 <sup>1</sup>	23.0±9.6	44.6±41.1 <sup>1</sup>	29.2±24.6	57.6±61.5	49.1±46.2
4	33.8±24.7 <sup>1</sup>	23.6±13.2	42.0±38.2 <sup>1</sup>	31.4±28.0	57.2±63.7	51.9±51.0
5	34.8±28.3 <sup>1</sup>	23.8±10.6	40.3±35.0 <sup>1</sup>	28.5±20.2	52.6±51.8	48.6±49.4

<sup>1</sup>p<0.05 compared to controls

**Table 3.** The frequency of abnormalities in aspartate aminotransferase (AST), alanine aminotransferase (ALT), and  $\gamma$ -glutamyltransferase (GGT) levels in workers with hepatitis and controls

The frequency of abnormal AST levels					
Year	Hepatitis workers		Controls		p
	The number of abnormal cases (%)	The number of normal cases (%)	The number of abnormal cases (%)	The number of normal cases (%)	
1	27 (21.8 %)	97 (78.2 %)	11 (4.4 %)	237 (95.6 %)	<0.01
2	26 (21.0 %)	98 (79.0 %)	13 (5.2 %)	235 (94.8 %)	<0.01
3	28 (22.6 %)	96 (77.4 %)	10 (4.0 %)	238 (96.0 %)	<0.01
4	27 (21.8 %)	97 (78.2 %)	12 (4.8 %)	236 (95.2 %)	<0.01
5	27 (21.8 %)	97 (78.2 %)	14 (5.6 %)	234 (94.4 %)	<0.01
The frequency of abnormal ALT levels					
1	45 (36.3 %)	79 (63.7 %)	59 (23.8 %)	189 (76.2 %)	<0.05
2	49 (40.0 %)	75 (60.0 %)	57 (23.0 %)	191 (77.0 %)	<0.01
3	51 (41.1 %)	73 (58.9 %)	57 (23.0 %)	191 (77.0 %)	<0.01
4	46 (37.1 %)	78 (62.9 %)	64 (25.8 %)	184 (74.2 %)	<0.05
5	48 (38.7 %)	76 (61.3 %)	54 (21.8 %)	194 (78.2 %)	<0.01
The frequency of abnormal GGT levels					
1	23 (18.5%)	101 (81.5%)	38 (15.3%)	210 (84.7%)	0.43
2	30 (24.2%)	94 (75.8%)	47 (19.0%)	201 (81.0%)	0.24
3	24 (19.4%)	100 (80.6%)	49 (19.8%)	199 (80.2%)	0.92
4	24 (19.4%)	100 (80.6%)	54 (21.8%)	194 (78.2%)	0.59
5	26 (21.0%)	98 (79.0%)	46 (18.5%)	202 (81.5%)	0.58

**Table 4.** Parameters in life history of workers with hepatitis engaged in hazardous works (HW) and usual works (UW)

		Workers with hepatitis engaged in HW	Workers with hepatitis engaged in UW	p
n		30	94	
Mean age		44.2±8.3	47.9±7.9	<0.05
Sex	Male	25	80	0.81
	Female	5	14	
Smoking	Smoker	16	36	0.15
	Non smoker	14	58	
Alcohol	> 20g/day	9	34	0.54
	< 20g/day	21	60	
Exercise	Yes	12	47	0.34
	No	18	47	
BMI		23.6±3.3	23.3±2.7	0.61

Data are expressed as mean±S.D., Significantly different compared to workers with hepatitis engaged in UW with respect to age.

the infection on the liver. Several reasons for such an outcome can be considered. The first reason might be that there is no standard set for workers, employers or their physicians to restrict working until serious liver dysfunction is detected. A second common reason is that patients with

HBV or HCV infection are carriers and are symptom free and for this reason, they do not seek treatment. They may even ignore liver dysfunction until serum aminotransferase level reaches its peak. A third reason, could be the fear of discrimination that would prevent the worker to seek

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**Table 5.** A comparison of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and  $\gamma$ -glutamyltransferase (GGT) levels in workers with hepatitis engaged in hazardous works (HW) with workers with hepatitis engaged in usual works (UW)

Year	Mean AST		Mean ALT		Mean GGT	
	Workers with hepatitis engaged in HW	Workers with hepatitis engaged in UW	Workers with hepatitis engaged in HW	Workers with hepatitis engaged in UW	Workers with hepatitis engaged in HW	Workers with hepatitis engaged in UW
1	45.2±37.5 <sup>1</sup>	32.5±23.8	74.1±118 <sup>1</sup>	39.3±40.9	56.5±66.5	44.2±54.6
2	42.6±36.0	35.3±26.1	62.0±69.7	44.3±48.0	59.7±68.6	49.9±51.4
3	44.0±32.0	34.5±27.6	58.8±45.8 <sup>1</sup>	40.1±38.7	57.6±61.5	49.1±46.2
4	39.9±27.9	31.9±23.4	56.6±47.1 <sup>1</sup>	37.3±33.9	57.2±63.7	51.9±51.0
5	38.9±29.3	33.5±28.0	50.3±35.4	37.1±34.4	52.6±51.8	48.6±49.4

<sup>1</sup>p<0.05 compared to workers with hepatitis engaged in UW

**Table 6.** The frequency of abnormalities in aspartate aminotransferase (AST), alanine aminotransferase (ALT), and  $\gamma$ -glutamyltransferase (GGT) levels in workers with hepatitis engaged in hazardous works (HW) and workers with hepatitis engaged in usual works (UW)

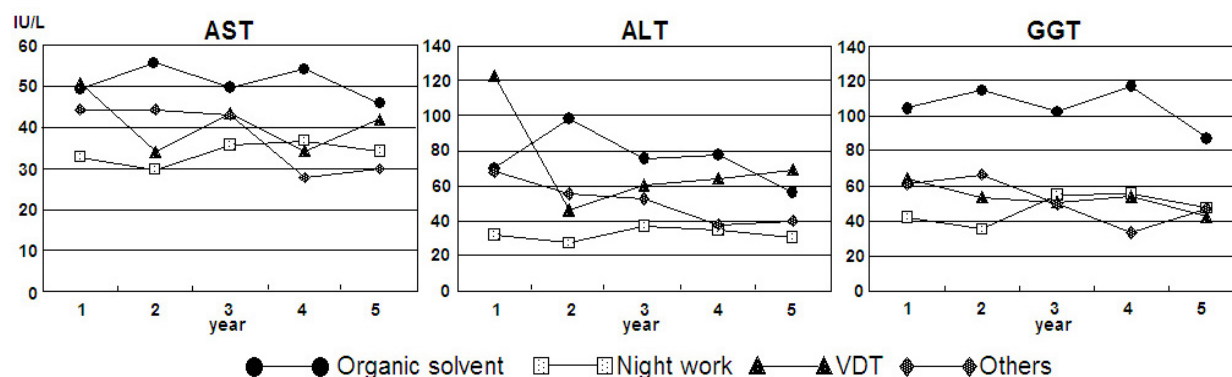
The frequency of abnormal AST levels					
Year	Workers with hepatitis engaged in HW		Workers with hepatitis engaged in UW		p
	The number of abnormal cases (%)	The number of normal cases (%)	The number of abnormal cases (%)	The number of normal cases (%)	
1	12 (40.0 %)	18 (60.0 %)	15 (16.0 %)	79 (84.0 %)	<0.01
2	8 (26.7 %)	22 (73.3 %)	18 (19.1 %)	76 (80.9 %)	0.38
3	10 (33.3 %)	20 (66.7 %)	18 (19.1 %)	76 (80.9 %)	0.11
4	11 (36.7 %)	19 (63.3 %)	16 (17.0 %)	78 (83.0 %)	<0.05
5	9 (30.0 %)	21 (70.0 %)	18 (19.1 %)	76 (80.9 %)	0.21
The frequency of abnormal ALT levels					
1	13 (40.3 %)	17 (59.7 %)	32 (34.0 %)	62 (66.0 %)	0.36
2	14 (46.7 %)	16 (53.3 %)	35 (37.2 %)	59 (62.8 %)	0.36
3	18 (60.0 %)	12 (40.0 %)	33 (35.1 %)	61 (64.9 %)	<0.05
4	18 (60.0 %)	12 (40.0 %)	28 (29.8 %)	66 (70.2 %)	<0.01
5	18 (60.0 %)	12 (40.0 %)	30 (31.9 %)	64 (68.1 %)	<0.01
The frequency of abnormal GGT levels					
1	8 (26.7 %)	22 (73.3 %)	15 (16.0 %)	79 (84.0 %)	0.19
2	8 (26.7 %)	22 (73.3 %)	22 (23.4 %)	72 (76.6 %)	0.72
3	7 (23.3 %)	23 (76.7 %)	17 (18.1 %)	77 (81.9 %)	0.53
4	9 (30.0 %)	21 (70.0 %)	15 (16.0 %)	79 (84.0 %)	0.09
5	7 (23.3 %)	23 (76.7 %)	19 (20.2 %)	75 (79.8 %)	0.71

**Table 7.** Parameters in life history of four groups categorized by hazardous works: 1) organic solvent, 2) night work, 3) visual display terminals (VDT), and 4) others (dust, lead, vibrations, and ionizing radiation)

		organic solvent	night work	VDT	others
n		10	6	7	7
Mean age		47.6±5.8	47.3±6.2	38.7±6.7	42.1±11.8
Sex	Male	8	4	7	6
	Female	2	2	0	1
Smoking	Smoker	6	5	3	2
	Non smoker	4	1	4	5
Alcohol	> 20g/day	3	2	1	3
	< 20g/day	7	4	6	4
Exercise	Yes	5	3	0	4
	No	5	3	7	3
BMI		23.9±3.5	22.8±3.7	23.6±2.6	23.7±2.6

**Table 8.** A comparison of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and  $\gamma$ -glutamyltransferase (GGT) levels of four groups categorized by hazardous works: 1) organic solvent, 2) night work, 3) visual display terminals (VDT), and 4) others (dust, lead, vibrations, and ionizing radiation)

Mean AST				
Year	Organic solvent	Night work	VDT	Others
1	49.3±28.0	32.7±13.8	50.9±66.7	44.3±28.3
2	55.8±37.8	29.8±16.3	34.0±29.2	44.4±50.0
3	49.8±26.7	35.8±21.4	43.4±39.0	43.1±43.2
4	54.3±41.2	36.7±21.6	34.3±13.6	27.7±8.6
5	45.9±45.4	34.3±19.2	42.0±21.1	29.9±9.1
Mean ALT				
1	69.8±53.2	32.0±16.9	122.7±235.7	67.9±54.4
2	98.5±95.3	27.3±13.6	46.1±35.2	55.4±68.4
3	75.4±55.3	36.8±20.6	60.4±43.5	52.4±48.0
4	77.7±67.6	35.0±20.7	64.0±39.1	37.7±16.9
5	56.1±41.1	30.5±20.6	69.3±43.6	40.0±16.9
Mean GGT				
1	104.8±118.2	42.5±35.0	64.6±81.6	61.3±70.5
2	114.7±112.5	35.8±23.7	53.9±48.9	66.6±101.8
3	102.7±105.9	55.5±55.5	51.0±38.3	50.0±49.3
4	117.5±117.7	55.8±51.3	54.3±31.2	33.7±12.4
5	87.6±86.7	47.8±53.2	42.7±15.8	47.3±44.9



**Figure 2.** Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and  $\gamma$ -glutamyltransferase (GGT) levels of four groups (workers with hepatitis involved with organic solvents, night work, VDT, and others including dust, lead, vibrations, and ionizing radiation).

**Table 9.** A comparison of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and  $\gamma$ -glutamyltransferase (GGT) levels in OS workers with hepatitis with OT workers with hepatitis

Year	Mean AST		Mean ALT		Mean GGT	
	OS workers	hepatitis	OS workers	hepatitis	OS workers	hepatitis
1	49.3 $\pm$ 28.0	43.1 $\pm$ 42.0	69.8 $\pm$ 53.2	76.3 $\pm$ 141.1	104.8 $\pm$ 56.8	56.8 $\pm$ 64.0
2	55.8 $\pm$ 37.8	36.1 $\pm$ 34.1	98.5 $\pm$ 95.3 <sup>1</sup>	43.8 $\pm$ 45.3	114.7 $\pm$ 112.5	52.9 $\pm$ 65.8
3	49.8 $\pm$ 26.7	41.1 $\pm$ 34.7	75.4 $\pm$ 55.3	50.1 $\pm$ 39.2	102.7 $\pm$ 105.9	52.0 $\pm$ 45.2
4	54.3 $\pm$ 41.2 <sup>1</sup>	32.7 $\pm$ 14.8	77.7 $\pm$ 67.6	46.1 $\pm$ 29.5	117.5 $\pm$ 117.7 <sup>1</sup>	47.6 $\pm$ 34.0
5	45.9 $\pm$ 45.4	35.5 $\pm$ 17.1	56.1 $\pm$ 41.1	47.4 $\pm$ 33.0	87.6 $\pm$ 86.7	45.9 $\pm$ 38.3

<sup>1</sup> p<0.05 compared to OT hepatitis workers, OS: organic solvent, OT: including night work, VDT, dust, lead, vibrations, and ionizing radiation

**Table 10.** The frequency of abnormalities in aspartate aminotransferase (AST), alanine aminotransferase (ALT), and  $\gamma$ -glutamyltransferase (GGT) levels in workers with hepatitis involved with organic solvents and workers with hepatitis not involved with organic solvents

The frequency of abnormal AST levels					
Year	OS hepatitis workers		OT hepatitis workers		p
	The number of abnormal cases (%)	The number of normal cases (%)	The number of abnormal cases (%)	The number of normal cases (%)	
1	5 (50.0 %)	5 (50.0 %)	7 (35.0 %)	13 (65.0 %)	0.46
2	5 (50.0 %)	5 (50.0 %)	3 (15.0 %)	17 (85.0 %)	0.08
3	5 (50.0 %)	5 (50.0 %)	5 (25.0 %)	15 (75.0 %)	0.23
4	5 (50.0 %)	5 (50.0 %)	6 (30.0 %)	14 (70.0 %)	0.43
5	3 (30.0 %)	7 (70.0 %)	6 (30.0 %)	14 (70.0 %)	1.0
The frequency of abnormal ALT levels					
1	5 (50.0 %)	5 (50.0 %)	8 (40.0 %)	12 (60.0 %)	0.71
2	6 (60.0 %)	4 (40.0 %)	8 (40.0 %)	12 (60.0 %)	0.44
3	6 (60.0 %)	4 (40.0 %)	12 (60.0 %)	8 (40.0 %)	1.0
4	7 (70.0 %)	3 (30.0 %)	11 (55.0 %)	9 (45.0 %)	0.69
5	7 (70.0 %)	3 (30.0 %)	11 (55.0 %)	9 (45.0 %)	0.69
The frequency of abnormal GGT levels					
1	4 (40.0 %)	6 (60.0 %)	4 (20.0 %)	16 (80.0 %)	0.38
2	6 (60.0 %)	4 (40.0 %)	2 (10.0 %)	18 (90.0 %)	<0.01
3	3 (30.0 %)	7 (70.0 %)	4 (20.0 %)	16 (80.0 %)	0.66
4	5 (50.0 %)	5 (50.0 %)	4 (20.0 %)	16 (80.0 %)	0.12
5	4 (40.0 %)	6 (60.0 %)	3 (15.0 %)	17 (85.0 %)	0.18

OS: organic solvent, OT: including night work, VDT, dust, lead, vibrations, and ionizing radiation

medical advice or treatment. Narai *et al.* has reported that 52.0% workers with hepatitis felt some level of anxiety about hepatitis and were worried not only about treatment but also discrimination in the workplace (17).

There are other studies that support our findings. Many studies have reported an association between liver disease and occupational factors. Shimizu H *et al.* reported that 5-nitro-o-toluidine exposure is associated with liver dysfunction (18). Wong RH *et al.* reported interactions between occupational vinyl chloride monomer exposure and

development of cancer in the liver of patients with HBV infection (19). On the other hand, Tabaru A *et al.* reported that there were no job-related factors that had any influence on the activity of hepatitis, although their study was relatively short (20). Although there have been no reports that overwork such as night work impairs serum aminotransferase levels, half of patients with chronic hepatitis C were fatigued (21-22). Further studies are required to determine how fatigue might impact the course of liver disease. Although the serum aminotransferase measurements were not significantly different among the

four groups, they were significantly different between the OS and OT groups. It is suggested that OS in HW worsens liver function of hepatitis workers. Luo JC *et al.* reported that a significant dose-response relationship existed between liver function abnormalities and dimethylformamide exposure and that HBV carrier status also had synergistic effects with dimethylformamide in causing liver abnormalities (23). Chen JD *et al.* reported that total serum bile acids are due to liver dysfunction used by solvent exposure (3). In this study, the major components of OS were xylene and toluene. Chen JD *et al.* suggested that increased GGT activity among workers was due to a higher level of exposure to the solvent mixture of xylene and toluene (24). Further study is required to clarify the relation that exists between serum aminotransferase levels and OS concentration in workers with hepatitis. The levels of serum aminotransferases increase by drinking. In this study, the alcohol consumption in subjects of 1<sup>st</sup> step, 2<sup>nd</sup> step and 3<sup>rd</sup> step as not significantly different from the alcohol consumption in controls of 1<sup>st</sup> step, 2<sup>nd</sup> step and 3<sup>rd</sup> step. The population of Japanese with HCV was twice as many as that of Japanese with HBV, although there were 86 people with HBV and 38 people with HCV in this study.

In conclusion, the higher mean serum level of AST and ALT in workers with hepatitis who were engaged in HW as compared to controls suggest that better monitoring and better standards should be developed to prevent the progression of chronic liver disease in these patients.

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**Abbreviations:** HBV: hepatitis B virus, HCV: hepatitis C virus, HW: hazardous works, UW: usual works, AST: aspartate aminotransferase, ALT: alanin aminotrasferase, GGT:  $\gamma$ -glutamyltransferase, VDT: visual display terminals, OS: organic solvent, OT: others works including night work, VDT, dust, lead, vibrations, and ionizing radiation

**Key Words:** Hepatitis B virus, Hepatitis C virus, Serum transaminase test, Aminotransferase, Hazardous works

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