Prevalence of problem drinking in patients with depression and association between depression severity and problem drinking: a cross-sectional survey

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ABSTRACT

Purpose: There has been little research into the effects of therapies for alcohol dependence in Japanese patients with depression and drinking problems. The aim of this study was to: 1) assess the prevalence of problem drinking in patients with depression and 2) evaluate the association between depression severity and problem drinking.

Methods: This cross-sectional survey was conducted in Japanese patients aged ≥ 20 years old with depression. Survey 1 identified those who engaged in habitual drinking and these individuals completed survey 2, which assessed alcohol consumption, depression severity and alcohol dependence or abuse.

Results: Overall, 2354 patients completed survey 1 and 425 patients completed survey 2. Of the patients who completed survey 2, 112 (26.4%; 95% confidence interval 22.2, 30.8) had alcohol dependence. Survey 2 showed that the severity of depression was significantly associated with the prevalence of alcohol dependence (p < 0.0001), suspected alcohol dependence (p = 0.0001) and high or very high drinking risk level (DRL; p < 0.0001). Univariate logistic regression analysis showed that alcohol dependence (p < 0.0001), suspected alcohol dependence (p = 0.0112), high DRL (p = 0.0027) and very high DRL (p = 0.0004) were significantly associated with severity of depression.

Conclusions: Among patients with depression who engaged in habitual drinking, the prevalence of alcohol dependence and suspected alcohol dependence were substantially higher than in the general population. Depression severity was significantly associated with alcohol dependence, suspected alcohol dependence and high or very high DRL.

Keywords: alcohol dependence, alcohol use disorder, depression, Japanese, survey

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Introduction

Worldwide, 7% and 13−18% of the general population experience current and lifetime problems with alcohol, respectively [1], while in Japan the prevalence of hazardous drinking is around 10%, with 1.1% of the population experiencing alcohol dependence in their lifetime [2].

Among patients with depression, approximately 16% have current problems with alcohol such as at-risk drinking, alcohol abuse and alcohol depend-
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ence, while approximately 30% experience such problems in their lifetime [1]. An association between depression and problem drinking has been recognized since 1990 [3, 4]; however, whether there is a causal relation remains to be established [5]. Sullivan and colleagues found that alcohol problems were associated with worse outcomes in some depression-related indexes [1], while other publications support these findings [6-8]. In Japan, a survey conducted among 775 patients with depression (285 men and 491 women) treated at general psychiatric institutions on an outpatient basis, showed that 8.8% of men and 4.7% of women had alcohol dependence [9]. However, to our knowledge there are few other studies that have investigated the association between alcohol dependence and depression in Japan.

The current study was undertaken to examine the relationship between depression and hazardous drinking specifically among Japanese individuals. The study had two aims; the first was to assess the prevalence of problem drinking in patients with depression, and the second was to evaluate the association between the severity of depression and problem drinking.

**Patients and Methods**

**Design and ethics**

This study was a cross-sectional survey conducted in patients 20 years old or older who had depression according to the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10), and were being treated at outpatient psychiatric clinics in Japan. Patients whose responses could not be considered credible were excluded (UMIN registration number UMIN 000025558).

This study was conducted in accordance with the protocol and the ethical principles outlined in the Declaration of Helsinki. The protocol was approved by the institutional review board in December 2016. Between 10 January 2017 and 30 May 2017, all patients provided verbal (survey 1) or written (survey 2) informed consent before entering the study.

**Assessments**

Survey 1 was administered to all eligible patients attending the outpatient psychiatric clinics and was designed to identify those who engaged in habitual drinking. Habitual drinking was defined as consumption of at least 180 mL of alcohol (sake or equivalent) per day for at least 3 days per week, which is the criterion for a drinking habit according to the National Health and Nutrition Survey by the Ministry of Health, Labour and Welfare of Japan.

Survey 2 was administered only to patients who met the criteria for habitual drinking in survey 1. Patient's sex, age, duration of depression, psychiatric comorbidities (schizophrenia, anxiety disorder, eating disorder, bipolar disorder, posttraumatic stress disorder, sleep disorder, drug dependence) and drinking guidance (whether the patient had been instructed to abstain from or reduce drinking, or had received no guidance) were obtained from medical records. Information about average daily alcohol consumption (amount of pure alcohol, g/day), number of days per month when alcohol consumption exceeded 60 g for men and 40 g for women, history of treatment for alcohol dependence, marital status and presence of physical comorbidities (hypertension, hyperlipidaemia, diabetes mellitus, hepatic disorder, gout, chronic pancreatitis, others) was collected during in-person interviews.

Patients who completed survey 2 were also assessed for severity of depression, presence of alcohol dependence or abuse, presence of alcohol use disorder, drinking risk level (DRL), health-related quality of life, work productivity and activity impairment, and their desire to improve the drinking habit. Severity of depression was assessed using the Sequenced Treatment Alternative to Relieve Depression (STAR*D) [10] version of the Structured Interview Guide for the Hamilton Depression Rating Scale (SIGH-D) [11], where scores 0–7 are normal, scores 8–13 indicate mild depression, 14–18 indicate moderate depression, 19–22 indicate severe depression, and scores higher than 23 indicate very severe depression. Severity of depression was also assessed by the Clinical Global Impression – Severity (CGI-S) scale [12]. Alcohol dependence and abuse were assessed using item J (alcohol dependence and abuse) of the Japanese version of the Mini International Neuropsychiatric Interview (MINI) questionnaire [13]. Patients who answered at least one of the questions 3a–d in the affirmative were diagnosed with alcohol abuse. Patients who answered at least three of the questions 2a–g in the affirmative were diagnosed with alcohol dependence. Alcohol use disorder was diagnosed using the Japanese version of the Alcohol Use Disor-
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Figure 1. Patient disposition

Survey 1

Enrolled (n=2806)

Study patients with informed consent (n=2354)

No informed consent (n=452)

Study patients of survey 1 (n=2354)

No data (n=0)

Patients with a drinking habit (n=487)

Survey 2

Study patients with informed consent for survey 2 (n=425)

No data (n=0)

Study patients of survey 2 (n=425)

ders Identification Test (AUDIT) [14]. Patients who scored 15 or higher were diagnosed with suspected alcohol dependence. DRL was determined using the World Health Organization methodology [4]. Health-related quality of life (HRQoL) was assessed using the EuroQol-5D (EQ-5D) questionnaire [15]. Work productivity and activity impairment (WPAI), specifically presenteeism, absenteeism and missed work hours due to health problems, were assessed using the Work Productivity and Activity Impairment Questionnaire: General Health (WPAI-GH), version 2.2 [16].

Primary and secondary outcomes

The primary outcome of this study was the prevalence of alcohol dependence, suspected alcohol dependence and alcohol abuse in patients with depression and habitual drinking. The secondary outcome was the association between the severity of depression and alcohol dependence, suspected alcohol dependence and abuse.

Statistical analysis

Prevalence was assessed by calculating the proportion of patients with alcohol dependence, suspected dependence and abuse and 95% CI. In addition, the proportions of patients with depression of each SIGH-D level were calculated in a post hoc analysis. The association between the prevalence of each SIGH-D level of depression and alcohol dependence, suspected alcohol dependence, alcohol abuse and DRL \( \geq \) high was assessed using the Cochran-Armitage Trend test. To evaluate the association between severity of depression and alcohol dependence or patients’ physical, social and psychological characteristics, a univariate logistic regression analysis was performed with SIGH-D score as the response variable (14 or higher vs lower than 14) and patient characteristics as the explanatory variable. Spearman’s rank correlation was used to assess the relationship between parameters of depression severity, drinking behaviour, HRQoL and work productivity and impairment. The significance level was set at 5% using a two-sided test. JMP version 11.0 or later, Microsoft Excel 2013 and SAS version 9.3 or later were used for statistical calculations.

Results

Survey results

Overall, 2354 patients with depression who were treated at 23 outpatient psychiatric clinics agreed to participate in survey 1 (Figure 1). Of these, 487 had a drinking habit and 425 agreed to participate in survey 2 (Table 1). The mean (standard deviation
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Table 1. Demographics of patients in survey 2

| Parameter                                           | Survey participants (n=425) |
|-----------------------------------------------------|----------------------------|
| Age (years), mean (range)                           | 48.1 (20.0-86.0)           |
| Male, n (%)                                         | 283 (66.6)                 |
| Duration of depression (years), mean (range)        | 3.75 (0.0-24.1)            |
| Psychiatric comorbidities, n (%)                    |                            |
| Schizophrenia                                       | 3 (0.7)                    |
| Anxiety disorder                                    | 97 (22.8)                  |
| Eating disorder                                     | 5 (1.2)                    |
| Bipolar disorder                                    | 33 (7.8)                   |
| Posttraumatic stress disorder                       | 4 (0.9)                    |
| Sleep disorder                                      | 125 (29.4)                 |
| Drug dependence                                     | 5 (1.2)                    |
| Other                                               | 12 (2.8)                   |
| None                                                | 190 (44.7)                 |
| Drinking guidance, n (%)                            |                            |
| Abstinence                                           | 31 (7.3)                   |
| Drinking reduction                                  | 153 (36.0)                 |
| No guidance                                         | 241 (56.7)                 |
| History of treatment for alcohol dependence, n (%)   | 15 (3.5)                   |
| Married, n (%)                                      | 247 (58.1)                 |
| Lives with others (family, partner, etc.), n (%)     | 307 (72.2)                 |
| Physical comorbidities, n (%)                       |                            |
| Hypertension                                        | 87 (20.5)                  |
| Hyperlipidaemia                                     | 36 (8.5)                   |
| Diabetes mellitus                                   | 24 (5.6)                   |
| Hepatic disorder                                    | 35 (8.2)                   |
| Gout                                                | 23 (5.4)                   |
| Chronic pancreatitis                                | 0                          |
| Other                                               | 48 (11.3)                  |
| None                                                | 264 (62.1)                 |
| Number of major depressive episodes, mean (range)    | 1.6 (0-10)                 |
| TAC (g/day), mean (range)                           | 37.78 (8.57-285.71)        |
| HDD (days/month), mean (range)                      | 8.60 (0.0-31.0)            |
| WHO Drinking Risk Level, n (%)                      |                            |
| Very high                                           | 32 (7.5)                   |
| High                                                | 43 (10.1)                  |
| Medium                                              | 88 (20.7)                  |
| Low                                                 | 262 (61.6)                 |

HDD, heavy drinking day; TAC, total alcohol consumption; WHO, World Health Organization.

[SD]) SIGH-D score for depression severity was 11.8 (7.2) in these 425 patients.

Prevalence of severe depression and alcohol dependence

Of the 425 patients included in survey 2, 44 patients (10.4%; 95% CI 7.6, 13.6) engaged in alcohol abuse, 112 patients (26.4%; 95% CI 22.2, 30.8) had alcohol dependence and 135 patients (31.8%; 95% CI 27.4, 36.4) had suspected alcohol dependence (Table 2).

The mean (SD) SIGH-D score was 16.5 (7.6) in patients with alcohol dependence (n = 112), 13.9 (7.8) in patients with suspected alcohol dependence (n = 135), 11.2 (5.9) in patients with alcohol abuse (n = 44) and 15.1 (7.7) in patients with high or very high DRL (n = 75). As the severity of depression increased there was a significant increase in the prevalence of patients with alcohol dependence (p < 0.0001), suspected alcohol dependence (p = 0.0001) and high or very high DRL (p < 0.0001), suggesting a significant association between depression and these drinking problems. On the other hand, there was no significant association between the severity of depression and the prevalence of al-
Table 2. SIGH-D scores and the number of patients with alcohol drinking problems

| SIGH-D score | Total | Alcohol dependence* | Suspected alcohol dependence** | Alcohol abuse* | Patients with DRL ≥High*** |
|--------------|-------|----------------------|-------------------------------|----------------|---------------------------|
| 0-7: Normal  | 425   | 112 (26.4%)          | 135 (31.8%)                   | 44 (10.4%)     | 75 (17.6%)                |
| 8-13: Mild depression | 135 | 15 (11.1%)          | 32 (23.7%)                   | 13 (9.6%)      | 14 (10.4%)                |
| 14-18: Moderate depression | 79 | 24 (30.4%)          | 21 (26.6%)                   | 10 (12.7%)     | 10 (12.7%)                |
| 19-22: Severe depression | 41 | 18 (43.9%)          | 21 (51.2%)                   | 4 (9.8%)       | 15 (36.6%)                |
| ≥23: Very severe depression | 41 | 29 (70.7%)          | 21 (51.2%)                   | 2 (4.9%)       | 15 (36.6%)                |
| Cochran-Armitage Trend test | – | <0.0001 | 0.0001 | 0.5815 | <0.0001 |

*Alcohol dependence and abuse were assessed using item J (alcohol dependence and abuse) of the Mini International Neuropsychiatric Interview (MINI) questionnaire, Japanese version. Patients who answered at least one of the questions 3a-d in the affirmative were diagnosed with alcohol abuse. Patients who answered at least three of the questions 2a-g in the affirmative were diagnosed with alcohol dependence.

**Suspected alcohol dependence was diagnosed using the Alcohol Use Disorders Identification Test (AUDIT), Japanese version. Patients who scored 15 or higher were diagnosed with suspected alcohol dependence.

***Patients not diagnosed with alcohol dependence, suspected alcohol dependence or alcohol abuse. DRL was determined using the World Health Organization methodology.

CI, confidence interval; DRL, drinking risk level; SD, standard deviation; SIGH-D, Structured Interview Guide for the Hamilton Depression Rating Scale.

Table 3. Univariate logistic regression analysis of factors associated with depression severity

| Category                              | Odds ratio | 95% CI     | p-value |
|---------------------------------------|------------|------------|---------|
| Age (vs individuals aged 1 year older) | 0.99       | 0.97, 1.00 | 0.1096  |
| Females (vs males)                    | 1.88       | 1.24, 2.84 | 0.0027  |
| Living with someone (vs living alone) | 0.77       | 0.50, 1.19 | 0.2373  |
| Marital status                        |            |            |         |
| Married/cohabiting (vs never married) | 0.73       | 0.45, 1.17 | 0.1879  |
| Single/living alone (vs married/cohabiting) | 1.57       | 0.86, 2.86 | 0.1411  |
| Physical comorbidities (vs no physical comorbidities) | 1.33       | 0.89, 1.98 | 0.1610  |
| Psychiatric comorbidities (vs no psychiatric comorbidities) | 1.00       | 0.67, 1.50 | 0.9985  |
| Alcohol abuse (vs no alcohol abuse) * | 0.93       | 0.49, 1.78 | 0.8264  |
| Suspected alcohol dependence (vs no suspected dependence) | 1.71       | 1.13, 2.60 | 0.0112  |
| Alcohol dependence (vs no alcohol dependence) | 4.29       | 2.72, 6.77 | <0.0001 |
| DRL ≥Medium (Medium + High + Very high) (vs Low) | 1.36       | 0.91, 2.03 | 0.1364  |
| DRL ≥High (High + Very high) (vs Medium + Low) | 2.16       | 1.31, 3.58 | 0.0027  |
| DRL ≥Very High (vs High + Medium + Low) | 4.02       | 1.85, 8.73 | 0.0004  |
| HDD ≥4 (vs ≤4) | 1.24 | 0.83, 1.83 | 0.2909  |

( ) represents denominator.

**"No alcohol abuse” included all patients except those with alcohol abuse, as diagnosed with MINI questionnaire. Analogous definitions applied to “no suspected alcohol dependence” and “no alcohol dependence”.

CI, confidence interval; DRL, drinking risk level; HDD, heavy drinking day

alcohol abuse (p = 0.5815; Table 2).

Variables associated with depression severity

Factors identified as being significantly associated with depression severity in the univariate logistic regression analysis were female sex (p = 0.0027), alcohol dependence (p < 0.0001), suspected alcohol dependence (p = 0.0112), high DRL (p = 0.0027) and very high DRL (p = 0.0004) (Table 3). Consistent with the analysis of prevalence, no association was found between depression severity and alcohol abuse (p = 0.8264).

Significant correlations were identified between total SIGH-D and CGI-S scores and the number of patients who gave affirmative answers to MINI question 2 (p = 0.0012 and p = 0.0019, respectively). Consciousness of a drinking problem was significantly associated with the total AUDIT score (p < 0.0001). The SIGH-D score was significantly
associated with EQ-5D \( (p = 0.0007) \), EQ-5D Visual Analogue Scale (EQ-5D-VAS; \( p = 0.0001 \) ), WPAI presenteeism \( (p = 0.0041) \), WPAI missed work hours due to health problems \( (p = 0.0042) \), CGI-S score \( (p < 0.0001) \) and sex \( (p < 0.0001) \) (Supplementary Table 1).

**Discussion**

The findings of this cross-sectional study show that the prevalence of habitual drinking in adult outpatients with depression was 20.7%. Among those patients who engaged in habitual drinking, the prevalence of alcohol dependence, suspected alcohol dependence and alcohol abuse was 26.4%, 31.8% and 10.4%, respectively. In this group, depression severity was significantly associated with alcohol dependence, suspected alcohol dependence and high or very high DRL. There was no significant association between severity of depression and alcohol abuse.

The prevalence of alcohol dependence in the Japanese general population was studied by Osaki and colleagues in 2003, 2008 and 2013 [2]. They defined alcoholism according to the AUDIT test, whereby a score of 15 or more denoted suspected alcoholism, and found a prevalence of 2.7% in 2013 [2]. Compared with these data, the prevalence of suspected alcohol dependence in patients with depression in the present study was 10 times higher. The prevalence of "current alcohol dependence" using ICD-10 diagnostic codes was 0.6% in the 2013 study by Osaki and colleagues and 26.4% in patients with depression in the present study (diagnosed with MINI). In a systematic review published in 2005, the median prevalence of current alcohol problems in patients with depression was 16% (range 5-67%), while it was 7% in the general population [1]. Comparable results were obtained in the present study.

The existence of a statistical association between alcohol use disorders and depression has been discussed since 1990 [3-5]. A meta-analysis of longitudinal and cross-sectional studies conducted by Boden and colleagues suggested the existence of this association and the authors concluded that it was robust to variations in study design and assessment methods [17]. The connection between alcohol use disorders and depression may be explained by a causal relation; however, this remained to be confirmed [17]. An analysis of the survey of a nationally representative population of 17,276 individuals conducted in Canada over a period of 12 years showed that this causal relationship is bidirectional in men, but not in women [18]. The results of a household survey of 43,083 individuals conducted in the US indicate that major depressive episodes are more strongly associated with alcohol dependence than with alcohol abuse [19]. These findings echo those of the present study, in which the severity of depression was significantly associated with alcohol dependence, but not abuse.

There is a debate about whether antidepressant treatments are less effective in patients with co-occurring depression and alcohol use disorder. In a meta-analysis of 14 randomized, double-blind, placebo-controlled clinical trials, antidepressants were found to produce a moderately-sized improvement in depressive symptoms (pooled effect size 0.38; 95% CI 0.18, 0.58) [20]. In a systematic review conducted by Foulds and colleagues, the pooled effect size of anti-depressant therapy compared to placebo was estimated at less than 0.2, with CI including zero [21]. In another systematic review that included controlled trials of antidepressants in patients with depression and alcohol dependence, antidepressants were shown to significantly improve some measures of alcohol dependence, although the quality of the included studies was low or moderate [22].

On the other hand, little research has been conducted on the effects of therapies for alcohol use disorders and it is possible that these therapies will lead to some improvement in depression in patients with co-occurring depression and alcohol use disorder. According to some estimates, up to 10% of the overall burden of major depression could be due to an alcohol use disorder [17]. One of the problems in the treatment of alcohol dependence is that abstinence is difficult to achieve and maintain, particularly in patients with comorbid depression. It would be interesting to investigate whether reducing alcohol consumption with the help of drugs would affect depression. The findings of the present study suggest that reducing alcohol consumption from high or very high DRL to moderate or mild could lead to reductions in the severity of depression. Further research into this area is warranted.

This study had a number of limitations. Firstly, patients with both independent and alcohol-induced depression were included in this study and all data
were analysed collectively. While the present study did not focus on the nature of causality, data on the natural histories of both disorders would be useful. Previous studies found sex differences in the prevalence of alcohol use disorders and depression [18]; however, the present study did not investigate these differences. Furthermore, no data on the use of treatments such as antidepressants, cognitive behavioural therapy, interpersonal psychotherapy or electroconvulsive therapy at baseline or during the study, which may confound the results was analyzed. Finally, because the present study was conducted exclusively in Japanese patients, the generalisability of its results may be limited in other populations.

Conclusions

The results of this study indicate that among patients with depression who engaged in habitual drinking the prevalence of alcohol dependence and suspected alcohol dependence were substantially higher than in the general population. In this group, depression severity was significantly associated with alcohol dependence, suspected alcohol dependence and high or very high DRL, but not with alcohol abuse. Further research into the effects of treatments for alcohol dependence, including on the symptoms of depression, is warranted.

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Author contributions

Susumu Higuchi conceived and designed the study. Yoshiyuki Shibasaki was the study statistician. Izuru Nakamura and Yoshiyuki Shibasaki contributed to the study design, preparation of the study report, writing of the manuscript, and read and approved the drafts. All authors participated in the interpretation of the data and in the writing, critical review and revision of the manuscript. All authors approved the final manuscript for publication.

CONFLICT OF INTEREST

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### Supplementary Table 1. Association between parameters in alcohol dependent patients. *Spearman’s rank correlation coefficient*

| Parameter | Correlation | p value |
|-----------|-------------|---------|
| M.N.I.Y to Q2 (n) | 0.3350 | 0.0003 |
| AUDIT (n) | 0.0196 | 0.4046 |
| SIGH-D total score | 0.8706 | <0.0001 |
| EQ-5D value | 0.3148 | 0.0007 |
| WPAI (present-symptoms) | 0.5059 | <0.0001 |
| WPAI (missed work hours due to health problem) | 0.3143 | 0.0183 |
| WPAI (abstinence) | 0.3720 | 0.0007 |
| WPAI (missed work hours due to health problem) | 0.0231 | 0.8658 |
| TAC | 0.7130 | 0.2000 |
| HDD | 0.3077 | 0.0280 |
| CGI-S | 0.1601 | 0.0918 |
| WPAI-GHY to Q1 | 0.0079 | 0.9338 |
| CGI-S | 0.6663 | 0.1017 |
| Marital status | 0.2200 | 0.3701 |
| Gender | 0.0197 | 0.3701 |
| History of treatment for alcohol dependence | 0.0639 | 0.5031 |
| Presence of physical complications | 0.0520 | 0.0875 |
| Presence of psychiatric complications | 0.0887 | 0.6365 |
| Satas of drinking during the drinking problem | -0.1707 | -0.1091 |
| Consciousness on the drinking problem | -0.1522 | -0.1091 |
| Consciousness to improve habitual drinking | 0.1091 |

**Legend:** AUDIT, Alcohol Use Disorders Identification Test; CGI-S, Clinical Global Impression - Severity; EQ, EuroQol; HDD, heavy drinking day; MNI, Mini International Neuropsychiatric Interview; Q; quarter of the year; SIGH-D, Structured Interview Guide for the Hamilton Depression Rating Scale; TAC, total alcohol consumption; VAS, visual analogue scale; WPAI-GHY, Work Productivity and Activity Impairment Questionnaire- General Health