

Relationship Between Mood Episode and Employment Status of Outpatients with Bipolar Disorder: Retrospective Cohort Study from the Multicenter Treatment Survey for Bipolar Disorder in Psychiatric Clinics (MUSUBI) Project

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Objective: The objective of this study was to clarify the relationship between mood episode and employment in patients with bipolar disorder to help improve their employment status.

Methods: All medical records of patients with bipolar disorder who visited 176 member clinics of the Japanese Association of Neuro-Psychiatric Clinics in September–October 2016 were investigated in September–October 2017. Details of the medical care received were investigated using a survey sheet, which included employment status. Odds ratios of mood episodes for employment status were analyzed using a logistic regression model.

Results: Among patients aged 60 years or less, 2292 described their occupation. On univariate analysis, odds ratios were statistically significant for depressive episode (OR = 2.68 [1.50–4.78] $p = 0.001$) and manic episode (OR = 2.64 [1.07–6.47] $p = 0.034$), whereas no significant difference was noted for mixed episode (OR = 1.72 [0.69–4.33] $p = 0.246$). On multivariate analysis, odds ratios were statistically significant for depressive episode (OR = 2.16 [1.13–4.13], $p = 0.020$) and manic episode (OR = 3.55 [1.36–9.25], $p = 0.010$), whereas no significant difference was noted for mixed episode (OR = 1.83 [0.65–5.14] $p = 0.254$).

Conclusion: Employment status among these patients with bipolar disorder receiving outpatient treatment was 43.5%. Compared to remission episodes, manic and depressive episodes were associated with a higher risk of unemployment.

Keywords: mood disorder, continuous employment, occupational health, Japan

Introduction

Since bipolar disorder develops at a young age and follows a chronic course through alternating cycles of manic, hypomanic and depressive episodes, many patients are required to balance treatment and work. The lifetime prevalence of bipolar disorder is said to be 0.4–3%.^{1,2} Bipolar disorder often begins in late adolescence to early adulthood, and the age of onset is typically in the late teens through the 20s.³ According to the results of the Global Burden of Disease Study, disability-adjusted life years (DALYs) are also evident from the teenage years, and peak in the 20s.⁴ Treatment is often difficult, and 50–60% of patients undergoing remission maintenance are said to relapse within several years.^{5,6} Under such circumstances, the proportion of patients with bipolar disorder who are able to

stay employed is reported to be 40–60%, and their employment rates are not high.^{7,8} Thus, bipolar disorder is a disease that occurs at a young age, involves cycles of mood episodes, and requires patients to balance continuous treatment and work.

Manic and depressive episodes are seen in bipolar disorder. Patients with bipolar disorder live a social life while experiencing these episodes, which creates a variety of difficulties. In brief, their activity levels increase during manic episodes and decrease during depressive episodes.⁹ In a mixed episode, manic and depressive symptoms occur simultaneously or in rapid succession.⁹

Patients with bipolar disorder live about half their life in a symptomatic state, primarily one of depressive symptoms, which may carry a risk of interfering with continuous employment.^{10,11} In patients with depressive symptoms, impairment of psychosocial function is more severe,^{12–14} and often prevents them from maintaining the ability to function at work.¹⁵ Patients with bipolar disorder have also been found to have functional impairment between episodes.^{16,17} Cognitive and working memory impairments are found in these functional disorders, and a relationship between these and employment disability has been noted.^{18,19} Functional impairment is reported to occur in the presence of psychotic symptoms, rapid cycling, psychiatric comorbidity, and substance abuse, which may affect employment.^{20–22} Bipolar patients live with these functional impairments, which can be obstructions to continuous employment.

These work-related problems concern not just the individuals themselves but society as well. The Global Burden of Disease Study attributed 8.4 million DALYs to bipolar disorder, and considered the condition to be a social burden.²³ In the United States, the social cost incurred by bipolar disorder is estimated to be \$45 billion per year.²⁴ When divided into direct (eg, medical and social service expenses) and indirect cost (eg, morbidity and mortality expenses), the direct cost is estimated to be \$7 billion and the indirect cost \$38 billion. Within the indirect cost, expenses associated with employment status, such as decreased productivity and unemployment, are estimated to be \$17 billion.²⁴ Given that Japan has about 120,000 patients with bipolar disorder, the need to develop measures is both a medical and a social issue.²⁵

Despite this mixture of medical and social issues, factors associated with continuous employment of patients with bipolar disorder are poorly known. Mood episode is one factor that may be linked to continuous employment.

The several guidelines for bipolar disorder formulated to date all describe a treatment approach for individual mood episodes,^{26–30} indicating the importance of identifying mood episodes when administering treatment for bipolar disorder. Regarding the relationship with employment, while depressive episodes have been linked to an increased risk of unemployment, no findings have been reported for manic or mixed episodes.^{16,31,32}

The objective of this study was to clarify the relationship between mood episode and employment in patients with bipolar disorder as a means of helping to improve their employment status.

Materials and Methods

Participants and Methods

The retrospective cohort investigation of the Multicenter Treatment Survey for Bipolar Disorder in Psychiatric Clinics (MUSUBI) projects^{33–37} was conducted at member clinics of the Japanese Association of Neuro-Psychiatric Clinics (JAPC). JAPC has 1650 member clinics, which examine about 30% of patients with mood disorders in Japan.³⁸ In this study, 176 of 1650 member clinics of JAPC took part in the survey. Investigators at these clinics are psychiatrists, most of whom are psychiatric specialists certified by the Japanese Society of Psychiatry and Neurology or designated psychiatrists certified by the Japanese Ministry of Health, Labour and Welfare. All medical records of patients with bipolar disorder who visited the 176 member clinics of the Japanese Association of Neuro-Psychiatric Clinics in September–October 2016 were investigated in September–October 2017. We gathered information about age, sex, psychiatric comorbidity, physical comorbidity, substance abuse, rapid cycling, psychotic symptoms, suicidal ideation, medication details and mood episodes (remission, depressive episode, manic episode, and mixed episode) in addition to employment status at two time points, October–December 2016 and October–December 2017. The diagnosis of bipolar disorder was based on the 10th Revision of the International Classification of Diseases and Related Health Problems (ICD-10). Clinical psychiatrists who participated in the survey completed the questionnaire through a retrospective medical record survey. The questionnaire included patient characteristics (age, gender, and occupational status), psychiatric and physical comorbidities, substance abuse, bipolar disorder subcategories, rapid cycling, mood episodes, psychotic symptoms,

suicide ideation, and details of pharmacological treatment. In this study, remission was defined as when the interviewing psychiatrist judged the patient to be in clinical remission with no depressive episodes, no manic episodes, and no mixed episodes. Episodes other than remission were also judged clinically. With respect to employment status, an individual who worked at least 30 hours a week was defined as a full-time worker. This criterion was noted on the survey form and was known to all participating psychiatrists prior to the start of the survey. An individual who was a full-time worker at baseline and still held a full-time job one year later was categorized as in “continuous employment,” and an individual who was a full-time worker at baseline but was unemployed one year later was categorized as “loss of employment.”

Ethics

This study was conducted in compliance with the Declaration of Helsinki and the Japanese Ethical Guidelines for Medical and Health Research Involving Human Subjects. This study was approved by the Ethics Committee of the Japanese Association of Neuropsychiatric Clinics and the Ethics Committee of Medical Research at the University of Occupational and Environmental Health. Since this was a retrospective investigation of medical charts, requirements pertaining to informed consent were waived. However, information on the study was disclosed on our web page, and patients were allowed to opt out.

Statistical Analysis

In the univariate analysis, logistic regression analysis was performed for each factor. Multivariate logistic regression analysis was then performed to avoid confounding effects of each factor. In the multivariate logistic regression analysis, the dependent variable was employment status. The odds ratios of mood episodes (remission, depressive episodes, manic episodes, and mixed episodes) for employment status were analyzed using a logistic regression model. The model included age, sex, psychiatric comorbidity, physical comorbidity, substance abuse, rapid cycling, psychotic symptoms, suicidal ideation, and medication details as confounding adjustment factors. Probability was set at the 5% level. The analyses were conducted using Stata SE/16 (StataCorp LLC, College Station, TX, USA).

Results

At baseline, the 176 clinics returned completed questionnaire sheets for 3137 outpatients with bipolar disorder. Descriptions of occupation were provided by 3081 of the 3137 patients. Of the 3081 patients, 2292 were under the age of 60, of whom 997 (43.5%) were full-time workers. Of these 997, 968 patients who were full-time workers aged under 58 years were included in the follow-up survey conducted one year later. In that survey, 816 patients (84.3%) participated, among whom 708 were still employed fulltime (= continuous employment) and 70 were unemployed (= loss of employment). Data of these 705 patients in the continuous employment group and the 70 in the loss of employment group are presented in Table 1. Between the groups, age and bipolar disorder subcategories were relatively similar, but differences were seen in other attributes, symptoms, and treatment details. Data by mood episode are shown in Table 2. Of the 775 patients, 398 patients were in remission, 268 were in a depressive episode, 50 were in a manic episode, and 59 were in a mixed episode. Data by mood episode are shown in Table 2. The two groups were relatively similar in age but differed in other attributes, symptoms and treatment details.

The results of univariate and multivariate analyses are shown in Table 3. In the univariate analysis, the odds ratio for unemployment was statistically significant for depressive episode (OR = 2.68 [1.50–4.78] $p = 0.001$) and manic episode (OR = 2.64 [1.07–6.47] $p = 0.034$). In contrast, no significant difference was noted for mixed episode (OR = 1.72 [0.69–4.33] $p = 0.246$). In the multivariate analysis, the odds ratio was statistically significant for depressive episode (OR = 2.16 [1.13–4.13] $p = 0.020$) and manic episode (OR = 3.55 [1.36–9.25] $p = 0.010$). Again, no significant difference was noted for mixed episode (OR = 1.83 [0.65–5.14] $p = 0.254$).

In the multivariate analysis, no significant difference was noted for physical comorbidity (OR = 0.68 [0.36–1.31] $p = 0.252$), substance abuse (OR = 0.19 [0.26–1.45] $p = 0.110$), or rapid cycling (OR = 0.55 [0.19–1.60] $p = 0.272$).

Discussion

This study was conducted to investigate employment status among patients with bipolar disorder and the impact of mood episode on their continuous employment. To our knowledge, only a few studies have explored the relationship between employment status and mood episode in

Table I Clinical Characteristics Between Patients with Continuous Employment and Loss of Employment

| | Continuous Employment | Loss of Employment |
|---|-----------------------|--------------------|
| | n=705 | n=70 |
| Sex, male(%) | 442(68%) | 23(33%) |
| Age(SD) | 44.6(8.7) | 42.9(10.1) |
| Psychiatric comorbidity | 117(17%) | 12(17%) |
| Physical comorbidity | 180(25%) | 13(19%) |
| Substance abuse | 41(6%) | 1(1%) |
| Bipolar Disorder Subcategories | | |
| Type I | 174(27%) | 17(24%) |
| Type II | 442(68%) | 48(69%) |
| Unclassifiable | 32(5%) | 5(7%) |
| Rapid cycling | 62(9%) | 4(6%) |
| Mood episode: n(%) | | |
| Remission | 375(53%) | 23(33%) |
| Depressive episode | 236(34%) | 32(46%) |
| Manic episode | 42(6%) | 8(11%) |
| Mixed episode | 52(7%) | 7(10%) |
| Psychotic symptom | 35(5%) | 7(10%) |
| Suicide ideation | 45(6%) | 8(11%) |
| Number of mood stabilizer prescriptions | | |
| 0 | 110(16%) | 15(21%) |
| 1 | 462(65%) | 37(53%) |
| 2 | 126(18%) | 15(21%) |
| 3 or more | 10(1%) | 3(4%) |
| Number of antipsychotics prescriptions | | |
| 0 | 376(53%) | 33(47%) |
| 1 | 265(37%) | 28(40%) |
| 2 | 67(10%) | 9(13%) |
| 3 or more | | |
| Number of antidepressant prescriptions | | |
| 0 | 401(57%) | 37(53%) |
| 1 | 240(34%) | 27(39%) |
| 2 | 63(9%) | 5(7%) |
| 3 or more | 3(0.4%) | 1(1%) |
| Number of anxiolytics prescriptions | | |
| 0 | 473(67%) | 36(51%) |
| 1 | 212(30%) | 28(40%) |
| 2 | 22(3%) | 6(9%) |
| 3 or more | 1(0.1%) | – |

(Continued)

Table I (Continued).

| | Continuous Employment | Loss of Employment |
|-----------------------------------|-----------------------|--------------------|
| | n=705 | n=70 |
| Number of hypnotics prescriptions | | |
| 0 | 329(47%) | 32(46%) |
| 1 | 236(33%) | 28(40%) |
| 2 | 137(19%) | 9(13%) |
| 3 or more | 6(1%) | 1(1%) |

Abbreviation: SD, standard deviation.

patients with bipolar disorder,^{16,31,32} and the present study is the first conducted in Japan. At baseline, 43.5% of the subjects were full-time workers. When we examined the impact of mood episode on the loss of employment, depressive episode and manic episode had a higher risk of unemployment than remission. The employment rate among patients with bipolar disorder has been reported to be 40–60% in studies published overseas,^{7,8} which is reasonably consistent from the result of our present study. Although only a handful of studies have investigated the relationship between mood episode and employment, some reported that depressive episode was a risk factor that may hinder continuous employment.^{16,31,32} With regard to the relationship between manic episode and employment, we found no conclusive studies.

In this study, patients with depressive episode had an increased risk of losing a job than those in remission. This is considered primarily attributable to functional reasons. A person with depressive episode may exhibit symptoms such as depressed mood, loss of interest/pleasure, weight loss/gain, decreased/increased appetite, insomnia/hypersomnia, psychomotor agitation/retardation, fatigue/listlessness, feelings of worthlessness and guilt, reduced thinking ability and concentration, difficulty in decision making, and suicidal ideation.⁹ These symptoms can delay work progress and frequently cause the person to show up late for work, leave work early, or be absent from work, leading to the loss of employment. In a depressive episode, the person's ability to function at work deteriorates, resulting in unemployment. To prevent such job loss and improve employment status among patients with bipolar disorder, the maintenance of remission is desired. However, even in remission, 70–90% of the patients with bipolar disorder are believed to relapse within 5 years,³⁹ and so the possibility of a recurrence of symptoms needs to be kept in

Table 2 Clinical Characteristics of Each Mood Episode

| | Total n=775 | Mood Episode | | | |
|-------------------------------|----------------|--------------------|-----------------------------|-----------------------|-----------------------|
| | | Remission n=398 | Depressive Episode n=268 | Manic Episode n=50 | Mixed Episode n=59 |
| Sex, male(%) | 65% | 67% | 69% | 54% | 47% |
| Age(SD) | 44.4(8.9) | 44.4(9.0) | 44.3(8.7) | 46.0(8.5) | 43.6(8.8) |
| Psychiatric comorbidity | 17% | 14% | 15% | 22% | 36% |
| Physical comorbidity | 25% | 21% | 25% | 32% | 46% |
| Rapid cycling | 9% | 6% | 9% | 12% | 21% |
| Psychotic symptom | 5% | 5% | 6% | 4% | 8% |
| Suicide ideation | 7% | 0% | 15% | 0% | 22% |
| Substance abuse | 5% | 3% | 8% | 6% | 12% |
| Mood stabilizer prescriptions | | | | | |
| 0 | 16% | 12% | 21% | 10% | 20% |
| 1 | 64% | 69% | 57% | 62% | 64% |
| 2 | 18% | 16% | 21% | 28% | 12% |
| 3 or more | 2% | 2% | 1% | 0% | 3% |
| Lithium | 47% | 50% | 44% | 56% | 36% |
| Valproic acid | 27% | 26% | 25% | 36% | 37% |
| Carbamazepine | 3% | 3% | 3% | 6% | 3% |
| Lamotrigine | 28% | 28% | 31% | 20% | 22% |
| Antipsychotics prescriptions | | | | | |
| 0 | 53% | 57% | 46% | 64% | 44% |
| 1 | 38% | 34% | 41% | 30% | 53% |
| 2 | 10% | 9% | 13% | 6% | 3% |
| 3 or more | 0% | 0% | 0% | 0% | 0% |
| Aripiprazole | 11% | 10% | 12% | 6% | 17% |
| Olanzapine | 21% | 18% | 25% | 14% | 19% |
| Quetiapine | 11% | 10% | 13% | 6% | 10% |
| Risperidone | 2% | 2% | 2% | 6% | 2% |
| Antidepressant prescriptions | | | | | |
| 0 | 56% | 65% | 42% | 75% | 55% |
| 1 | 34% | 29% | 46% | 19% | 44% |
| 2 | 9% | 7% | 11% | 6% | 2% |
| 3 or more | 1% | 0% | 1% | 0% | 0% |
| Anxiolytics prescriptions | | | | | |
| 0 | 65% | 72% | 54% | 72% | 64% |
| 1 | 31% | 25% | 40% | 26% | 34% |
| 2 | 4% | 3% | 5% | 2% | 2% |
| 3 or more | 0% | 0% | 0% | 0% | 0% |
| Hypnotics prescriptions | | | | | |
| 0 | 46% | 54% | 38% | 40% | 36% |
| 1 | 34% | 29% | 38% | 34% | 46% |
| 2 | 19% | 16% | 22% | 26% | 19% |
| 3 or more | 1% | 1% | 1% | 0% | 0% |

(Continued)

Table 2 (Continued).

| | Total n=775 | Mood Episode | | | |
|--------------------------------|----------------|--------------------|-----------------------------|-----------------------|-----------------------|
| | | Remission n=398 | Depressive Episode n=268 | Manic Episode n=50 | Mixed Episode n=59 |
| Bipolar Disorder Subcategories | | | | | |
| Type I | 25% | 27% | 20% | 34% | 27% |
| Type II | 69% | 67% | 75% | 62% | 63% |
| Unclassifiable | 6% | 5% | 6% | 4% | 10% |

Abbreviation: SD, standard deviation.

Table 3 Association Between Mood Episode and Continuous Employment

| Mood Episode | n | Loss of Employment(%) | Univariable | | | Multivariable* | | | | |
|--------------------|-----|-----------------------|-------------|-------------------|---------|----------------|-------------------|---------|------|-------|
| | | | Odds Ratio | 95% Conf Interval | P value | Odds Ratio | 95% Conf Interval | P value | | |
| Remission | 398 | 6 | Reference | | | Reference | | | | |
| Depressive episode | 236 | 12 | 2.68 | 1.50 | 4.78 | 0.001 | 2.16 | 1.13 | 4.13 | 0.020 |
| Manic episode | 42 | 16 | 2.64 | 1.07 | 6.47 | 0.034 | 3.55 | 1.36 | 9.25 | 0.010 |
| Mixed episode | 52 | 12 | 1.72 | 0.69 | 4.33 | 0.246 | 1.83 | 0.65 | 5.14 | 0.254 |

Notes: *Adjustment factors: age, sex, psychiatric comorbidity, physical comorbidity, substance abuse, rapid cycling, psychotic symptoms, suicide ideation, pharmacotherapy.

mind. It is important to recognize a depressive episode at an early stage and initiate an intervention. Although bipolar disorder shares the same depressive symptoms as major depressive disorder (MDD), treatment for depression differs from that for the depression phase of bipolar disorder. Additionally, patients with bipolar disorder are reported to have more severe work impairment than those with MDD.⁴⁰ Therefore, it is important to be aware that bipolar disorder should be examined with even greater care than MDD.

Manic episode was also found to be associated with a higher risk of unemployment than remission. The increased risk of unemployment in patients with manic episode is considered attributable to both social and functional reasons. A person with manic episode may exhibit symptoms such as inflated and exaggerated self-esteem, decreased desire for sleep, talkativeness or urgency, flight of ideas, distraction, increased goal-oriented activities, psychomotor agitation, and engagement in activities that could be potentially troublesome.⁹ Distraction causes the person to become unable to pay attention to details at work, leading to increased mistakes. Flight of ideas causes the person to undertake different tasks one after another, leaving them all unfinished. Inflated self-esteem causes the person to take on reckless challenges and become arrogant and uncooperative. In a manic episode, the person's ability

to function at work deteriorates in this manner, resulting in unemployment. Unlike people with depressive episode, those with manic episode may also lose their job for social reasons in addition to functional decline. To prevent unemployment in this manner, it is also important to recognize manic episode at an early stage and initiate an intervention, as with depressive episode.

Although no gender difference is thought to exist in the course of bipolar disorder, the proportion of men in our present study was higher in the continuous employment group. In comparison, a survey by the Ministry of Health, Labor and Welfare reported an employee turnover rate for full-time workers in Japan in 2019 of 13.4% for men and 18.2% for women, and thus higher for women.⁴¹ This result is therefore considered to reflect the social gender difference in Japan. The percentages of psychotic symptoms and suicidal ideation were lower in the continuous employment group. However, there was no difference in the percentage of psychiatric comorbidity, while the percentages of physical comorbidity, substance abuse, and rapid cycling were higher in the continuous employment group than in the loss of employment group. These symptoms and comorbidities are considered to be factors for a poor prognosis in bipolar disorder and are unlikely to contribute to continuous employment.⁴² We consider that these results are likely to be affected by unmeasured bias.

In the future, it is considered necessary to conduct studies on these symptoms, comorbidities and continuous employment.

Limitations

Several limitations of our study warrant mention. First, due to the relatively short retrospective follow-up period (1 year), the risk of long-term unemployment is unknown. Considering the treatment duration for bipolar disorder, investigation over a longer period is desirable.

Second, although the retrospective one-year follow-up rate was relatively good, at 84%, the impact of dropouts is unknown. When baseline characteristics were compared between dropouts and follow-up completers, there was no difference in sex, age, manic episode, or mood stabilizer or antipsychotic use. While depressive episode and mixed episode were more common in dropouts, antidepressants, psychiatric comorbidity, and psychotic symptoms were more common in follow-up completers.

Third, since this study focused on the relationship between mood status at baseline and unemployment, the modified effects of treatment details, concomitant symptoms, and detailed comorbidities are unknown. In particular, as treatment details are clinically managed by the patients' primary physicians, the impact of specific treatment regimens is unknown. This study considered factors such as drug therapy, but did not consider blood concentrations of mood stabilizers or non-drug therapies such as psychotherapy.

Fourth, because this study was conducted in parallel with daily clinical practice, the assessment was conducted as a single interview, and a structured clinical interview was not required. Accordingly, although the assessments were conducted by well-trained physicians, the presence of inter-rater variability cannot be ruled out.

Fifth, baseline functioning was not assessed, and rating scales such as the Hamilton Depression Rating Scale (HAM-D), Montgomery Åsberg Depression Rating Scale (MADRS), and Young Mania Rating Scale (YMRS) were not used, which may have made the assessment less accurate.

Sixth, the characteristics of this study may limit its generalizability to other populations. In Japan, employees are allowed to take leave due to illness. This period may vary among workplaces and may range from a few months to several years. During this period, the employee will generally not receive any salary, but will be entitled to receive an injury and illness allowance from the health

insurance association for a period of one year and six months. This applies to all workers, but some companies offer more generous guarantees of their own. The system for leave of absence differs among countries, which may undermine the external validity of our results in countries other than Japan.

Conclusion

In the MUSUBI-J-Study, 43.5% of patients with bipolar disorder undergoing outpatient treatment were full-time workers. Depressive and manic episodes were associated with higher risk for unemployment than remission. Employment rates among patients with bipolar disorder need to be improved. In patients with bipolar disorder who work in a depressive or manic episode, the risk of future unemployment is high; therefore, an appropriate intervention should be provided.

Approval of the Research Protocol

This study was approved by the Ethics Committee of the Japanese Association of Neuropsychiatric Clinics (ID: 20160822, 20180723) and the Ethics Committee of Medical Research at the University of Occupational and Environmental Health, Japan (approval no. UOEHCRB20-112).

Informed Consent

Information on the study was disclosed on our web page, and patients were allowed to opt out.

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Disclosure

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