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Outcome of bipolar mood disorder treatment in elderly patients in tertiary care hospital like BSMMU

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Abstract

Introduction: Bipolar disorder is a recurrent and long term mental illness that can seriously affect the lives of patients and their families. Globally the lifetime prevalence of all forms of the illness, often referred to as bipolar spectrum disorders, has been estimated to be 5% in the general population. **Objective:** To assess the Outcome of Bipolar mood disorder treatment in elderly patients in tertiary care hospital. Methods: A prospective cohort study was conducted between July 2022 to October 2023 in a tertiary care teaching hospital BSMMU located in Shahbag, Dhaka Bangladesh. The Institutional Ethics Committee approval was obtained before the study. All newly diagnosed bipolar disorder patients as per diagnostic and statistical manual-IV criteria or previously diagnosed bipolar disorder patients but not on treatment and who are willing to participate in the study were enrolled. **Results:** During the study period, 100 bipolar disorder patients were enrolled in the study based inclusion criteria. Patient demography, age at onset, treatment outcome, and other details are summarized in Table 1. The average age of the study population was 37.6 ± 14.1 years (mean ± SD), and 65.0% (n = 65) of the patients were female. Early-onset bipolar disorder was seen in 17.0%, (n = 17) and the mean age at early-onset bipolar disease was 15.7 ± 2.4 (mean ± SD) years. Treatment delay was observed in 24.0% (n = 24) of patients. At the end of the follow-up period, 38.0% (n = 38) had remission and 76% (n = 76) had non remission. There was a statistically significant (at $P < 0.01$), 67.5% reduction in YMRS and 70.0% reduction HAM-D score compared to baseline whereas in nonremission group, reduction in YMRS and HAM-D score was not significant. However, remission (45.7%, n = 16) was more in patient who were treated with mood stabilizers (lithium salts) compared to anticonvulsants (31.2%, n = 19) and antipsychotics (30.0%, n = 21). Twelve variables were analyzed to identify the possible association with nonremission in the study population. Early onset (OR: 9.77; confidence intervals [CI]: 1.11–86.01), treatment delay (OR: 6.48; CI: 1.27–32.92) treatment noncompliance (OR: 4.64; CI: 1.37–15.64), and single living (OR: 4.26; CI: 1.56–11.66) were independently associated with nonremission in bipolar disorder patients. Other variables, namely low income, depression, male sex, hypothyroidism, hypertension, and obesity also had OR >1; however, they were not statistically significant. Smoking and alcoholism shown to favour remission but again results were statistically no significant.
Conclusion: It is known that the outcome of bipolar disorder treatment is highly variable and several patients and environmental-related factors may affect the outcome. The identified factors may be used as a clinical decision supporting tool and addressing these factors in the early phase of treatment may reduce the chances of nonremission in bipolar disorder patients and improve their quality of life.

Keywords: bipolar affective disorder, effect, knowledge

Introduction

Bipolar disorder is a recurrent and long term mental illness that can seriously affect the lives of patients and their families. Globally the lifetime prevalence of all forms of the illness, often referred to as bipolar spectrum disorders, has been estimated to be 5% in the general population [1, 2].

Ganguli *et al*. reported that the national rate of affective disorder in India as 34 per 1000 population [3]. Bipolar disorder is one

of the most common psychiatric illnesses with cyclic changes in mood from mania or hypomania to depression or vice versa. In bipolar disorder, the patient's cognitive and behavioral abilities are affected, at work or school as well as daily chores in the household [4]. The symptoms, course, severity, and response to treatment vary among individual patients. Alcohol and substance abuse is common among patients with bipolar disorder and can have a significant impact on the age of onset, course of the illness, and response to treatment [5]. Bipolar disorder is highly misdiagnosed at times, which leads to comorbid conditions and delayed treatment of the same. Due to this, bipolar disorder is often hard to treat and leaves the patient with prolonging disabilities such as unemployment and mental retardation. If left untreated, there is an increased risk of suicide, morbidity, and mortality [4]. Furthermore, the treatment outcomes in bipolar disorder are highly variable, and the treatment must be individualized as the clinical presentation, severity, and frequency of episodes vary widely among each patient. Early recognition of the factors affecting the treatment outcome will help the treating physicians to early implementation of individualized treatment and a better clinical outcome.

Materials and Methods

A prospective cohort study was conducted between July 2022 to October 2023 in a tertiary care teaching hospital BSMMU located in Shahbag, Dhaka Bangladesh. The Institutional Ethics Committee approval was obtained before the study. All newly diagnosed bipolar disorder patients as per diagnostic and statistical manual-IV criteria or previously diagnosed bipolar disorder patients but not on treatment and who are willing to participate in the study were enrolled. The patients were followed for 6 months from the day of enrolment. Patients who are not willing to undergo treatment, without clear treatment outcome as remission or nonremission and patients who lost the follow-up were excluded from the study. Patient demography, age at bipolar disorder was diagnosed, age at treatment was started, social habits, signs and symptoms, medical and psychiatric comorbidities, treatment paten, and compliance to treatment were recorded in predesigned case record form.

Outcome measures

The Young mania rating scale (YMRS) and Hamilton Depression Rating Scale (HAM-D) scores were used to measure the severity of manic episodes and depression, respectively, in the study population, at baseline, and at last follow-up. YMRS and HAM-D were assessed by expert psychiatrists in the presence of the investigator. Based on the changes in YMRS and HAM-D scores from baseline to the last follow-up, the patients were classified into remission and nonremission.

Definitions

Early onset is defined as bipolar disorder diagnosed before 18 years of age [6]. Remission is described as that clinical stage wherein the patient does not exhibit any symptoms of mania or depression with a YMRS ≤12 and HAM-D score of seven or less [7, 8]. Nonremission is that clinical stage where the patient exhibits signs and symptoms of mania or depression irrespective of being on prescribed medication [9]. Low-income group is defined, as total annual household income is between 1 and 2 lakh [10]. The single living is defined as unmarried, widowed or divorced condition and living separately. Treatment delay is defined as when the interval between the onset of bipolar disorder and its first treatment is >6 years [11].

Statistical analyses

Nominal data were described and expressed in frequency and percentage. Parametric data were expressed as the mean ± standard deviation (SD). Comparison of YMRS/HAM-D scores at baseline and last follow-up was done using paired *t*-test. Multiple logistic regression was used to identify risk factors associated with nonremission in bipolar disorder patients and calculation of odds ratio (OR). In multiple logistic regression, factors were selected based on published literatures and clinical relevance as judged by expert clinicians. Factors having less than adequate number of events (<10) per independent variable were not included in the multiple logistic regression analysis. P <0.05 was considered as statistically significant for all analyses. Data entry and statistical analysis were done using IIBM SPSS version 20.0 (IBM Corp. IBM SPSS Statistics for Windows, Armonk, NY).

Results

During the study period, 100 bipolar disorder patients were enrolled in the study based inclusion criteria. Patient demography, age at onset, treatment outcome, and other details are summarized in Table 1. The average age of the study population was 37.6 ± 14.1 years (mean ± SD), and 65.0% (n = 65) of the patients were female. Early-onset bipolar disorder was seen in 17.0%, (n = 17) and the mean age at early-onset bipolar disease was 15.7 ± 2.4 (mean ± SD) years. Treatment delay was observed in 24.0% (n = 24) of patients. At the end of the follow-up period, 38.0% (n = 38) had remission and 76% (n = 76) had non remission.

Table 1: Demography, clinical characteristics and outcome of bipolar patients (n=100)

Characteristics	Total number of bipolar Patients
Age (years), Mean ±SD	37.6±14.1
Female, n (%)	65(65.0)
Smoking, n (%)	30 (30.0)
Alcohol, n (%)	11 (11.0)
Early-onset, n (%)	17 (17.0)
Age at early onset (years), mean ±SD	15.7±2.4
Treatment delay, n (%)	24 (24.0)
Remission, n (%)	38 (38.0)
Non remission, n (%)	76(76.0)

Subtypes of bipolar disorder based on specific mood episodes are summarized in Table 2, majority of the patients (75.0%, n = 75) were diagnosed with Bipolar I disorder, followed by Bipolar II disorder (7.0%, n = 7), cyclothymic disorder (1.0%, n = 1), and mixed features (17.0%, n = 17).

Table 2: Types of bipolar disorder (n=100)

Types	Frequency (%)
Bipolar I disorder	75 (75.0)
Bipolar II disorder	7 (7.0)
Cyclothymic disorder	1 (1.0)
Mixed features	17 (17.0)

Mean YMRS and HAM-D scores among remission and nonremission group at the last follow-up are shown in Table

3. There was a statistically significant (at $P < 0.01$), 67.5% reduction in YMRS and 70.0% reduction HAM-D score compared to baseline whereas in nonremission group, reduction in YMRS and HAM-D score was not significant.

Table 3: Bipolar disorder severity scores among remission and non-remission group (n=100)

Bipolar Disorder Severity	Remission group			Non remission group		
	Baseline	Follow-up	Decrease (%)	Baseline	Follow-up	Decrease (%)
YMRS	26.8±6.5	8.7±2.5*	67.5	27.4±5.1	18.3±5.2	33.0
HAM-D	22.0±4.4	6.6±1.7*	70.0	23.6±4.4	15.7±5.01	33.0

Drug treatment pattern among the study population is shown in Table 4. Antipsychotics (70.0%, n = 70 were the most the most commonly prescribed agents followed by antidepressant (61.0%, n = 61). However, remission (45.7%, n = 16) was more in patient who were treated with mood stabilizers (lithium salts) compared to anticonvulsants (31.2%, n = 19) and antipsychotics (30.0%, n = 21).

Table 4: Different type of treatment in bipolar disorder patients (n=100)

Drugs	Frequency (%)	Outcome	
		Remission, n (%)	Non remission, n (%)
Mood stabilizers (Lithium Salts)	35 (35.0)	16 (45.7)	19 (54.3)
Antipsychotics (Quetiapine)	70 (70.0)	21 (30.0)	49 (70.0)
Anticonvulsants (Divalproex Sodium)	61 (61.0)	19 (31.2)	42 (68.8)
Antidepressants (Sertraline)	62 (62.0)	16 (25.8)	46 (74.2)

The results of multiple logistic regression are summarized in Table 5. Twelve variables were analyzed to identify the possible association with nonremission in the study population. Early onset (OR: 9.77; confidence intervals [CI]: 1.11–86.01), treatment delay (OR: 6.48; CI: 1.27–32.92) treatment noncompliance (OR: 4.64; CI: 1.37–15.64), and single living (OR: 4.26; CI: 1.56–11.66) were independently associated with nonremission in bipolar disorder patients. Other variables, namely low income, depression, male sex, hypothyroidism, hypertension, and obesity also had OR >1; however, they were not statistically significant. Smoking and alcoholism shown to favor remission but again results were statistically nonsignificant.

Table 5: Identification of factors associated nonremission in bipolar disorder patients (n=100)

Risk factor	Nonremission, n (%)	Remission, n (%)	OR	95% CI	P
Early onset	15 (94.0)	1 (6.0)	9.77	1.11-86.01	0.040*
Treatment delay	21 (91.3)	2 (8.7)	6.48	1.27-32.92	0.024*
Treatment noncompliance	25 (86.2)	4 (13.8)	4.64	1.37-15.64	0.013*
Low in-come(<taka 5000/month	44 (72.2)	17 (27.8)	1.77	0.67-4.68	0.253
Depression	9 (81.8)	2 (18.2)	1.84	0.33-10.26	0.487
Single living	41 (83.7)	8 (16.3)	4.26	1.56-11.66	0.005*
Male sex	34 (70.8)	14 (29.2)	2.36	0.73-7.64	0.153
Smoking	19 (67.8)	9 (32.2)	0.50	0.12-2.19	0.360
Alcohol dependence	7 (70.0)	3 (30.0)	0.55	0.89-3.47	0.434
Hypothyroidism	11 (78.6)	3 (21.4)	1.86	0.39-8.86	0.865
Hypertension	10 (71.4)	4 (28.6)	1.14	0.26-4.91	0.132
Obesity	8 (80.0)	2 (20.0)	1.41	0.20-10.15	0.962

Discussion

In this study, 100 bipolar disorder patients were followed for 6 months from the day of enrollment into the study. As per our knowledge and literature search, it is the first study attempted to identify the factors leading to nonremission in bipolar disorder patients. The mean age of our study population was 37.6 ± 14.1 years with female predominance; (56.2%) these observations were similar to the results published in a study conducted by Perry *et al*., in that study, the mean age was 43 ± 15 years with female patients being 68% [12]. The incidence of bipolar disorder is more in female gender may be due to their lifestyle or physiological effects. A study conducted by Leibenluft showed that women are more prone to suffering from bipolar disorder as compared to men [13]. In our study population, 14.9% had the early-onset bipolar disorder and mean age at early onset was 15.7 ± 2.4. Early-onset bipolar disorder is most common, in a study conducted by Post *et al*. 50% of the patient had early-onset disease [14]. According to the American Psychiatric Association and according to Wells *et al*., the average age of the onset of first manic episode is about 21 years, our results also showed a similar pattern [4]. According to a study conducted by Mc Glashan, it showed that with the passing of adolescence, the disorder becomes less penetrating with respect to virulence. Conversely, late-developing mania or late onset of illness, even if it is mild, may be devastating to someone with established rigid, defensive styles and less adaptive flexibility [15]. Treatment delay and implications: According to Post *et al*., treatment delay occurs when the patient starts his/her medication much after the disorder is diagnosed. This can cause resistance to drugs and positive outcome with the treatment would be affected [14]. In our study, bipolar disorder Type I has found to be more common although there is no substantial literature support. This may be due to the smaller sample size of our study. Although studies have suggested that bipolar disorder Type I is more severe and acute when compared to the other types while bipolar Type II patients have a more chronic course of

treatment, significantly more depressive episodes, and shorter periods of being well between episodes than patients with bipolar disorder I, also there is a high risk for suicide [16]. A wide range of medical comorbidities have been observed in various studies on bipolar population. According to Kupfer, the most common being cardiovascular disease, obesity, and diabetes mellitus [17]. Literature by Fagiolini *et al*. showed that 49% suffered from abdominal obesity, suggesting that metabolic disorders are risky and very high in the prevalence of bipolar patients [18]. F, according to McElroy *et al*., obesity in bipolar disorder may be due to factors such as age, gender, binge eating problems, income level, psychotropic drugs that cause weight gain, geographical location, and health habits [19]. There was a statistically significant (at $P < 0.01$), 67.5% reduction in YMRS and 70.0% reduction HAM-D score compared to baseline, A study conducted by Kauer-Sant'Anna *et al*. reported 34% functionality recovery in 6 months, in patients with a first psychotic episode, 33% of those had functional recovery after 3 years of follow-up [20]. Medications prescribed for bipolar disorder, in our study, showed that 76 (62.8%) patients prescribed with atypical antipsychotics, 67 (55.4%) patients were given antidepressants. Surprisingly, antipsychotic agents were used more frequently than mood stabilizers. A study conducted by Blanco *et al*. showed that there had been a decrease in the use of mood stabilizers and an increase in the use of atypical antipsychotics and anticonvulsants particularly valproates. Antipsychotics are being prescribed more often now for manic and mixed type of episodes. They have lesser side effects and do not produce extrapyramidal syndrome. Antidepressants are commonly prescribed in the absence of mood stabilizers [21]. Risk factors associated nonremission found to have a significant effect were early onset, treatment delay, noncompliance, and single living. Noncompliance is seen in all age groups. The reason for this is polypharmacy, forgetfulness, and lack of education regarding the illness. According to Colom *et al*. noncompliance leads to increase the risk of relapse, decrease in quality of life, increase in symptoms, and more suicidal attempts. About 20%–60% of bipolar patients are noncompliant. One-third of the bipolar patients do not consume 70% of their medication. This leads to increase relapse rates causing the poor outcome [22]. Another significant risk factor found in our study was marital status, more specifically the unmarried, separated and widowed patients. According to Yoshimasu *et al*. and Krishnan, this may be because of lack of family support leading to depression, substance abuse, suicide attempts. Unmarried, separated, and widowed patients socially isolate themselves. A lack of family and social support leads to an increase in suicidal attempts [23, 24].

Conclusions

It is known that the outcome of bipolar disorder treatment is highly variable and several patients and environmental-related factors may affect the outcome. The identified factors may be used as a clinical decision supporting tool and addressing these factors in the early phase of treatment may reduce the chances of nonremission in bipolar disorder patients and improve their quality of life.

Conflicts of interest

None.

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