

# Course and Outcome of Adolescent-onset Bipolar Affective Disorder: a Retrospective Clinic-based Study

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## Abstract

**Objective:** This study examined the course and outcome of adolescent-onset bipolar affective disorder.

**Patients and Methods:** Case records of patients who had attended the study centre between 1989 and 1996 were screened and records of patients who met the study criteria were included.

**Results:** For most patients enrolled in the study, the first affective episode was mania and the majority had psychotic features. The median time for resolution of mania was 5 weeks and this was influenced by the presence of psychotic symptoms. The mean time for the first recurrence was 23 months and this was not influenced by any of the study variables. There was no difference between patients whose first episode was mania and those with depression for age of onset, gender, duration of illness at contact, and time for the resolution of the first episode. However, patients who had depression had a greater number of episodes.

**Conclusion:** Adolescent patients developing an affective episode should have regular long-term monitoring.

*Key words:* Adolescent-onset bipolar disorder, Course, Depression, Mania, Outcome

## Introduction

A significant proportion of patients with bipolar affective disorder develop their illness during childhood or adolescence.<sup>1,2</sup> Recent studies report prevalence rates of bipolar affective disorder of 0.2% to 0.4% and 1.0% in children<sup>3</sup> and adolescents,<sup>3,4</sup> respectively.

A growing body of literature indicates that, in comparison to adults, adolescents with bipolar disorder have more severe affective episodes and a high rate of mixed episodes and psychotic features,<sup>5</sup> increased rates of co-morbidity with other disorders,<sup>4,6</sup> and a positive family history.<sup>5,7</sup> In addition, the course of adolescent-onset bipolar disorder also differs from that of adult-onset illness. Except for 1 study,<sup>8</sup> research suggests that juvenile age of onset of bipolar illness is often associated with frequent recurrences,<sup>7,9-11</sup> particularly if the first affective episode is mixed or cycling<sup>9,10</sup> or a depressive episode,<sup>7</sup> or there is chronicity<sup>4</sup> or a poor response to lithium prophylaxis.<sup>5</sup>

The consequences often associated with younger age of onset of bipolar affective disorder include increased social morbidities such as interruption of education, marital problems,<sup>7</sup> and poor functioning.<sup>4</sup> Although the issue is critical, only a few studies have examined the course and outcome of adolescent-onset bipolar affective disorder in detail. In a community study addressing the prevalence, phenomenology, co-morbidity, and course of bipolar disorder in older adolescents, compared with patients with depression, bipolar patients were found to have a chronic course.<sup>4</sup> In a clinic-based study of 54 adolescents with bipolar I disorder, 96% had recovered from the index episode.<sup>10</sup> One or more relapses were noted in 44% of the patients and none of the factors were found to be predictive of both the recovery from the first episode and relapses. In another hospital-based study comprising 30 patients with a **DSM-III-R** diagnosis of bipolar disorder, recovery from the index episode was noted in all patients (100%).<sup>11</sup> Approximately 67% had one or more relapses of affective disorder and, notably, there was also no predictor of recovery or relapse in this study.

The existing studies have a few limitations, including lack of examination of possible predictors of recovery and remission,<sup>4</sup> inclusion of patients whose index episode was not the first affective episode<sup>10,11</sup> (as the prediction of the course of affective disorder from the first episode has more clinical relevance), and no examination of the influence of treatment on the rate of recovery.<sup>10,11</sup> Therefore, the present

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study was preformed to document the course and outcome of adolescent-onset bipolar affective disorder.

## Patients and Methods

The study was conducted at the Central Institute of Psychiatry, Ranchi, India. In this hospital, all new patients are first examined by junior resident doctors and then by consultant psychiatrists as routine clinical practice. Psychiatric diagnoses are made according to the *International Classification of Diseases (ICD) Diagnosis of Mental and Behavioral Disorders*. This study was a case-review study performed according to the following procedure.

Case records of patients registered between 1989 and 1996 were screened. Records of patients meeting the following study criteria were included:

- adolescent patients aged 11 to 19 years whose first affective episode was treated at the study centre and who had subsequently received the diagnosis of either ICD-10<sup>12</sup> bipolar affective disorder (F31.0-F31.8) or ICD-9<sup>13</sup> manic-depressive psychosis, circular type (296.2, 296.3, 296.4) [patients with unspecified bipolar/manic-depressive psychosis were excluded]
- adolescent patients who had a minimum of 2 years of follow-up since studies have reported an increased rate of recurrences during the first 24 months after the first episode<sup>10,11</sup>
- patients who had been followed-up at least to the end of adolescence (at least 19 years), as evidenced by the conversion of case records from child psychiatry to adult psychiatry.

Case notes of patients who did not meet the above criteria and whose case notes contained inadequate demographic and clinical details were excluded. Recovery and relapse was defined according to Strober et al, as follows:<sup>10</sup> a patient was considered recovered when he/she maintained a period of at least 8 consecutive weeks with no more than 2 affective symptoms of mild intensity; and relapse was defined as the occurrence of a new episode of illness satisfying Research Diagnostic Criteria (RDC)<sup>14</sup> for mania or depression. In this study, compliance was defined as good when medication adherence was approximately 75% and above during the follow-up period.

## Data Analysis

Statistical analysis was done with the standard software package (SPSS Windows Version 10.1). Group differences were examined with Fisher's exact test and Mann-Whitney U test. Kaplan-Meier survival analysis was done to examine the difference between the patients whose first episode was mania versus depression in terms of rate of remission from the first episode and the time for the first recurrence. Breslow statistics were used to examine the differences in the survival distributions. Cox regression model was used to examine the effects of covariates on the rate of remission from the first episode and the rate of the first recurrence.

## Results

### Sociodemographic Profile

Twenty seven case notes of adolescents met the study criteria. The mean duration of follow-up was 4.8 years (standard deviation [SD]  $\pm$  1.8 years; range, 2 to 9 years). The mean age of the patients at the time of first contact was 14.96 years. Most patients were men, were literate, and were from rural lower income backgrounds. Of the 27 patients, 7 had a family history of an affective disorder (4 [14.8%] had bipolar disorder and 3 [11.1%] had non-bipolar disorders) and 4 (15.4%) had a history of delayed developmental milestones. None of the patients had co-morbid psychiatric disorders such as conduct disorder (Table 1).

### Clinical Characteristics

The mean age of onset of the first episode was 14.77 years and mania was the first affective episode for most patients. At least 1 psychotic feature was noted in 16 patients. Of the 18 patients who received a mood stabilising agent along with either an antipsychotic agent or antidepressant, 14 received lithium and 4 received lithium and carbamazepine. Eighteen patients had been admitted to hospital for the first episode. The median and mean duration of the first episode at the time of the first consultation was 4.00 and 4.68 weeks, respectively. Remission was noted in all 27 patients — the median and mean times taken for the resolution of the first episode after treatment was 5.00 and 6.35 weeks, respectively. The mean duration of follow up was 57.5 months. The mean time until the first recurrence was 23 months and the mean number of manic, depressive, and total episodes were 2.40, 1.03, and 3.48, respectively. Eight patients (29.6%) had 1 recurrence, 7 (25.9%) had 2 recurrences, 7 (25.9%) had 3 recurrences, 3 (11.1%) had 4

**Table 1. Sociodemographic profile.**

Variable	Number of patients (%)
Age at contact (years) [mean $\pm$ SD]	14.96 $\pm$ 1.01
Sex	
Male	24 (88.9)
Female	3 (11.1)
Education	
Illiterate	3 (11.1)
Literate	24 (88.9)
Residence	
Rural	19 (70.4)
Urban	6 (22.2)
Semi-urban	2 (7.4)
Income (rupees/month)	
$\leq$ 2000	22 (81.5)
2001-5000	5 (18.5)
$\geq$ 5001	0 (0.0)
Family history of affective disorders	7 (25.9)
Bipolar disorders	4 (14.8)
Non-bipolar disorders	3 (11.1)
Delayed milestones	4 (15.4)

recurrences, 1 (3.7%) had 5 recurrences, and 1 (3.7%) had 7 recurrences. A comparison of the rate of remission of the first episode and the time for the first recurrence between patients whose first episode was mania and those whose first episode was depression is shown in Figures 1 and 2. Most patients had received combination therapy with mood stabilising agents for the management of subsequent episodes. Analysis with Cox regression model revealed that, except for psychosis, none of the other variables such as age of onset, sex, developmental history, duration of first episode, type of first episode, and nature of treatment had an impact on the rate of remission (Table 2).

### Differences in Clinical Profiles According to Type of First Episode

There were non-significant differences between patients whose first episode was mania versus depression for age of

onset of the first affective episode (Mann-Whitney U test,  $z = -1.214$ ;  $p = 0.23$ ), sex (Fisher's exact test,  $p = 0.53$ ), duration of first episode at first contact (Mann-Whitney U test,  $z = -0.459$ ;  $df = 0.66$ ), and time for remission of the first episode (Mann-Whitney U test,  $z = -0.327$ ;  $p = 0.74$ ) [Figure 1]. Although the time for first recurrence of patients who had depression as their first episode seemed to be different from that of patients who had mania as a first episode (Figure 2), the difference was statistically non-significant (Mann-Whitney U test,  $z = -1.303$ ;  $p = 0.20$ ). Lack of significant differences between patients whose first episode was mania versus depression in the survival distributions of the time for the first episode of remission and the time for the first recurrence was confirmed by the Breslow statistics. The mean number of episodes was found to be greater in patients whose first episode was depression (Mann-Whitney U test,  $z = -2.521$ ;  $df = 0.01$ ). Presence of psychotic features was

Table 2. Clinical profile.

Variable	Number of patients (%)
<i>Characteristics of first episode</i>	
Age of onset (years) [mean ± SD]	14.77 ± 1.08 (range, 13-16)
Duration of the first episode before treatment (weeks) [mean ± SD]	4.68 ± 2.7 (range, 1-12; median, 4)
Polarity	
Mania	19 (70.4)
Depression	8 (29.6)
Presence of psychosis	16 (59.3)
Nature of treatment	
Antipsychotics/antidepressants	5 (19.2)
Antipsychotics/antidepressants with mood stabilisers	18 (65.4)
Electroconvulsive shock therapy	4 (15.4)
Time taken for remission (weeks) [mean ± SD]	6.35 ± 4.40 (range, 1-16) (median time: 5 weeks)
Number admitted to hospital	18 (66.7)
<i>Characteristics of subsequent episodes</i>	
Time for the first recurrence (months) [mean ± SD]	23.25 ± 22.20 (range, 0-79)
Number of episodes	
Mania	2.4 ± 1.05 (range, 1-5)
Depression	1.03 ± 1.29 (range, 0-5)
Total	3.48 ± 1.45 (range, 2-8)
Nature of treatment of the last episode	
Antipsychotics/antidepressants with mood stabilisers	17 (63.0)
Mood stabilisers alone	8 (29.6)
Electroconvulsive shock therapy	2 (7.4)
Compliance	
Poor	6 (22.2)
Good	21 (77.8)

Figure 1. Differences between groups in the rate of remission of the first episode.

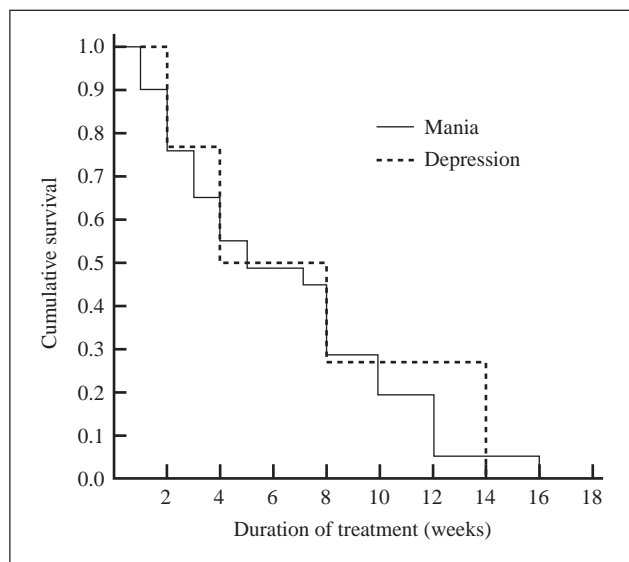
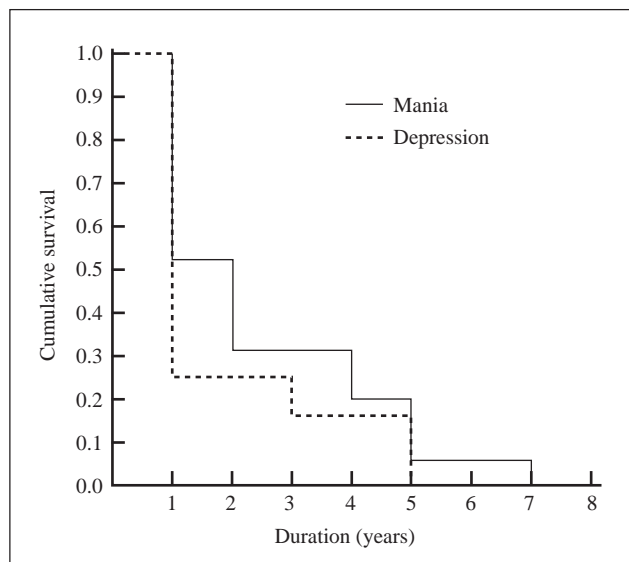


Figure 2. Differences between groups in time for first recurrence.



**Table 3. Differences between patients with first episode of mania or depression.**

Variable	Polarity of the first episode	
	Mania Number of patients (%)	Depression Number of patients (%)
Age of onset of the first episode (years) [mean $\pm$ SD]	14.94 $\pm$ 1.02	14.37 $\pm$ 1.18
Sex		
Male	16 (66.7)	8 (33.3)
Female	3 (100)	0 (0)
Family history of affective disorders	5 (26.3)	2 (25.0)
Duration of the first episode (weeks) [mean $\pm$ SD]	4.89 $\pm$ 2.9	4.0 $\pm$ 1.78
Time for remission of the first episode (weeks) [mean $\pm$ SD]	6.21 $\pm$ 4.3	7.0 $\pm$ 5.2
Psychotic features	15 (78.9)	1 (12.5)
Admission to hospital	16 (84.2)	2 (25.0)
Nature of treatment of first episode		
Antipsychotics/antidepressants	3 (15.8)	2 (28.6)
Antipsychotics/antidepressants with mood stabilisers	15 (78.9)	2 (11.8)
Electroconvulsive shock therapy	1 (5.3)	3 (42.9)
Time for the first relapse (months) [mean $\pm$ SD]	26.16 $\pm$ 22.95	16.37 $\pm$ 20.01
Total number of episodes	3.00 $\pm$ 1.05	4.62 $\pm$ 1.69

seen more frequently among patients whose first episode was mania (Fisher's exact test,  $p = 0.002$ ). A greater number of patients whose first episode was mania received mood stabiliser combination therapy whereas electroconvulsive therapy was more frequently given for patients whose first episode was depression. Examination of the factors influencing the first recurrence by Cox regression model revealed that none of the variables such as age of onset, sex, developmental history, duration of the first episode, polarity of the first episode, presence of psychotic features, and nature of the treatment had an influence on the time for the first recurrence (Table 3).

## Discussion

Sample characteristics such as gender difference, education, income status, and background status indicate the general characteristics of the patient population attending the present study centre. In this study, a family history of bipolar and non-bipolar affective disorders was noted in approximately 15% and 11% of the patients, respectively. While the rate of family history of bipolar disorders was comparable, the rate of non-bipolar disorders noted in the present study was slightly higher than that found in the study by Srinath et al.<sup>11</sup> Except for the present study, none of the other studies<sup>4,10</sup> has documented a history of delayed developmental milestones among the patients. This issue needs to be examined further. The rate of co-morbidity noted in Srinath et al's study<sup>11</sup> is significantly lower than that of prior studies.<sup>4,10</sup> The fact that none of our patients had any co-morbid conditions supports this previous study<sup>11</sup> and suggests that perhaps Indian adolescents with bipolar illness may be less prone to developing co-morbid psychiatric illnesses. However, this proposition requires further validation with cross-cultural data.

While this study, agrees with Srinath et al's study,<sup>11</sup> it differs from those of other authors,<sup>4,10</sup> including those performed in western populations, with regard to the mean age of onset, the nature of the first episode, and the presence of psychotic symptoms. Although the duration of the affective episode prior to the consultation and the time required for remission after treatment was comparable between the present study and the study by Srinath et al,<sup>11</sup> this finding is significantly shorter than that of Strober et al's study.<sup>10</sup> In both the earlier studies,<sup>10,11</sup> recovery from the index episode was not found to be influenced by different demographic and clinical variables. Likewise, except for psychotic features, none of the demographic and clinical characteristics of patients had an impact on the rate of remission in the current study. The present finding that the presence of psychotic symptoms influenced the remission rate of the first episode may be explained by the fact that, in the study by Srinath et al,<sup>11</sup> the impact of psychosis on the remission rate was not included and, in the study by Strober et al,<sup>10</sup> the proportion of patients who had psychosis was smaller. However, as to how the presence of psychotic symptoms negatively affects outcome, further examination is needed.

In Strober et al's study, approximately 23%, 13%, and 8% of the patients had 1, 2, and 3 recurrences, respectively.<sup>10</sup> Although the rate of a single recurrence was almost comparable to that of Strober et al,<sup>10</sup> the rates of 2 and 3 recurrences were found to be higher in the present study. While the rate of 2 recurrences was lower than in the Srinath et al study,<sup>11</sup> the rates of 3 or more recurrences were found to be higher in the present study. Since approximately 77.8% of patients in the present study had good compliance, the noted discrepancies may not be attributable to the regularity of medication intake alone.

The proportion of patients who had the first recurrence during the first and second years of remission were comparable between the current study and Srinath et al's study.<sup>11</sup> Similar to the other studies,<sup>10,11</sup> no influencing factor for recurrence could be identified in the present study. These findings suggest that patients who had their first episode should be regularly followed up for at least 2 years after the remission of the first episode.

In Strober et al's study, both the duration of the index episode and the time for remission were longer among patients whose index episode was depression.<sup>10</sup> Although the duration of the first episode was comparable between groups in the present study, the time required for remission of the first episode was longer in the group that had depression as the first episode. However, this finding was statistically non-significant, similar to that of Srinath et al's study.<sup>11</sup> Similar to other studies,<sup>10,11</sup> a group difference for the rate of relapse between patients whose first episode was mania versus depression was not seen. However, the mean number of episodes was found to be significantly greater among patients whose first episode was depression as opposed to mania. This finding is not consistent with the finding of Srinath et al.<sup>11</sup> Notably, a high proportion of patients with first episode mania had psychotic symptoms in the current study. The significance of this finding needs further exploration, even though the presence of psychotic features had no influence on the recurrence rates in the present study.

In summary, because the rate of relapse within the first 2 years of the index episode is high, as noted in both this study and Srinath et al's study,<sup>11</sup> regular monitoring of adolescent patients for at least 2 years after the index episode is essential. Furthermore, the present study indicates that patients whose first episode was depression require close attention, as this group is likely to experience more episodes in the long term. This study has some limitations such as small sample size, purposive sampling, and retrospective design. In addition, analysis of patients who had less than 2 years of follow-up could have helped to understand the reasons for shorter follow-up. The present study may be considered to be a naturalistic follow-up study because treatment approaches were uncontrolled. Further studies including patients with first affective episode will enhance the understanding of the outcome of adolescent-onset bipolar disorder. Outcome studies should also couple functional outcome measures such as scholastic performance, occupational functioning, quality of life, and mortality rates

with clinical outcome measures to obtain a clear picture of the prognosis of adolescent-onset bipolar disorders.

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