

# The Index Manic Episode in Juvenile-Onset Bipolar Disorder: The Pattern of Recovery

J Rajeev, MD<sup>1</sup>, Shoba Srinath, DPM, MD<sup>2</sup>, YCJ Reddy, DPM, MD<sup>3</sup>, MG Shashikiran, MD<sup>4</sup>, Satish Chandra Girimaji, MD<sup>5</sup>, Shekhar P Seshadri, DPM, MD<sup>5</sup>, DK Subbakrishna, PhD<sup>6</sup>

**Objective:** Recent studies of patients with juvenile bipolar disorder report low rates of recovery and high rates of chronicity. However, we lack data on the short-term outcome. This study examines the pattern of recovery from the index episode in an aggressively treated juvenile sample.

**Method:** We assessed 25 subjects (< 16 years) with a diagnosis of mania, using the Diagnostic Interview for Children and Adolescents-Revised (DICA-R), Young Mania Rating Scale (YMRS), and Children's Global Assessment Scale (CGAS) at intake and at 3 and 6 months. We studied the time taken to recover from the index episode, the level of functioning, and the factors predicting them.

**Results:** After 6 months, 24 (96%) subjects had recovered from the index manic episode. The median time to recovery was 27 days. Total episode length was significantly longer among those with previous affective episodes.

**Conclusions:** The findings suggest that juvenile-onset mania has high rates of recovery and low rates of chronicity. These differences from the existing literature need further exploration.

(Can J Psychiatry 2003;48:52–55)

Author affiliations appear at the end of the article.

## Clinical Implications

Juvenile-onset mania has high recovery rates, which could possibly be due to early and aggressive treatment.

Recovery rates for juvenile-onset mania are better in study populations consisting predominantly of adolescents and those with low rates of comorbidity.

The high recovery rate is at some variance with the available literature. It is possible that differences in sample characteristics may explain this variance.

## Limitations

The sample size was small.

The sample was not controlled for medication.

The rater was not blind to the patients' clinical and medication status.

**Key Words:** bipolar disorder, course, juveniles, children, adolescents, comorbidity

Prospective studies of bipolar disorders (BDs) in children and adolescents are few and the findings conflict. While some studies report excellent recovery rates from index bipolar episodes (1,2), other studies report low recovery rates, ranging from 14% to 65% (3–6). No predictors of recovery were identified in any of these studies, with the exception of 1

study that reported longer episodes in those with comorbid attention-deficit hyperactivity disorder (ADHD) (3).

This study examined the recovery pattern over a period of 6 months in subjects with index manic or mixed affective episodes, assessed their level of global functioning, and attempted to identify predictors of recovery and functioning.

**Table 1** Baseline demographic and clinical characteristics of the sample

Characteristic ( <i>n</i> = 25)	Value
Sex	
Female, <i>n</i> (%)	10 (40)
Male, <i>n</i> (%)	15 (60)
Age at intake (years), mean (SD)	14.1 (1.4)
Age at onset (years), mean (SD)	13.7 (1.7)
Drug-naïve at intake, <i>n</i> (%)	19 (76)
Prepubertal (< 13 years) onset, <i>n</i> (%)	3 (12)
Index episode as first episode, <i>n</i> (%)	16 (64)
First-episode polarity, <i>n</i> (%)	
Manic	17 (68)
Depressive	4 (16)
Mixed affective	4 (16)
Type of index episode, <i>n</i> (%)	
Manic	21 (84)
Mixed affective	4 (16)
Psychotic symptoms, <i>n</i> (%)	15 (60)
Mood congruent, <i>n</i> (%)	12 (80)
Comorbid psychiatric condition, <i>n</i> (%)	9 (36)
Attention-deficit hyperactivity disorder	1 (4)
Oppositional defiant disorder	7 (28)
Conduct disorder	1 (4)
Avoidant disorder of childhood	1 (4)
Hospitalization for the index episode, <i>n</i> (%)	20 (80)
Duration of hospital stay (days), mean (SD)	28 (21)

## Methods

The sample comprised all the consecutively presenting children and adolescents aged under 16 years who satisfied DSM-III-R criteria for manic or mixed-affective episode. The sample was recruited from the Child and Adolescent Psychiatry (CAP) Services of the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India, between January 1, 1998, and May 31, 1999.

This was a protocol-driven study, and all subjects followed the stated protocol. After we obtained informed consent, we evaluated the subjects and their parents or guardians. Subjects were evaluated initially using a topical format (7) and subsequently using the Diagnostic Interview for Children and Adolescents-Revised (DICA-R) (unpublished), the Young Mania Rating Scale (YMRS) (9), and the Children's Global Assessment Scale (CGAS) (10). The DICA-R is a revised version of the DICA (8) that follows DSM-III-R diagnosis criteria. We administered the DICA-R to confirm the diagnosis of mania, to identify past episodes of affective illness, to establish first-episode polarity, and to diagnose lifetime comorbid psychiatric conditions. When we interviewed either parent, we used the parent version in addition to the child-adolescent

version. The information obtained from all the sources was reviewed, and 2 experienced child psychiatrists established a consensus diagnosis. The subjects were reassessed by the same investigator at 3 and 6 months, using the DICA-R, YMRS, and CGAS. All subjects received the standard treatment prescribed by the CAP Services, which includes monthly follow-ups and counselling regarding the need for regular medication. The study did not control for this.

Recovery from the index episode was defined as the absence of relevant DSM-III-R symptoms or, if present, not more than 2 affective symptoms of mild intensity, with maintenance of the foregoing state for a minimum 8-week interval (1,2). We analyzed the cumulative probability of recovery from the index episode, the level of global functioning, and the predictors of recovery and functioning. The statistical measures selected, based on the sample size, were the Kaplan-Meier survival curve, the log-rank test, and repeated-measures analysis of variance (RMANOVA).

## Results

Out of 817 patients at the CAP Services newly registered during the study period, 26 subjects had mania (3.2%). One dropped out, and 25 subjects completed the study. For 22 (88%) subjects, this was the first-ever psychiatric consultation. Table 1 gives the baseline demographic and clinical characteristics of the sample.

All subjects received lithium carbonate for treatment of the index episode, and 21 (84%) continued to receive lithium until the end of the study period. The mean dosage of lithium was 1074 mg daily, and serum level was maintained in the therapeutic range (0.8 to 1.2 mEq/L). Three subjects (12%) did not respond to lithium, and 1 (4%) did not tolerate it. Of the nonresponders, 2 received sodium valproate (mean dosage 1150 mg daily). The subject who did not tolerate lithium received carbamazepine (800 mg daily). In 1 nonresponder, the index episode did not remit during the course of the study. Nonresponse to lithium was defined as < 50% reduction of YMRS scores after at least 4 weeks of lithium treatment at therapeutic levels. Fourteen subjects (56%) needed neuroleptic medication in addition to mood stabilizers. Three (12%) of these patients did not respond to the combination and needed electroconvulsive therapy (ECT). They were given 9 to 11 modified unilateral ECTs on alternate days. All 3 responded to ECT. Clonidine (50 µg daily) was used to treat 1 patient who had comorbid ADHD. All patients continued to receive regular medication until the end of the study period.

All subjects had an acute onset (less than 2 weeks) of the index episode. The median duration at the time of presentation was 30 days (mean 32 days, SD 27). The median total duration of the index episode from onset to recovery was 60 days (mean 70 days, SD 44).

**Table 2 YMRS<sup>a</sup> and CGAS<sup>b</sup> scores over the course of the study period**

Scores <sup>c</sup>	At intake	At 3 months	At 6 months	RMANOVA <sup>d</sup>	
				F-ratio	P
YMRS, mean (SD)	39.2 (7.5)	5.1 (7.5)	3.0 (7.3)	164.2	< 0.0001
CGAS, mean (SD)	23.2 (9.3)	73.9 (17.7)	82.0 (15.1)	140.9	< 0.0001

<sup>a</sup>Young Mania Rating Scale (10)  
<sup>b</sup>Children's Global Assessment Scale (11)  
<sup>c</sup>At the 3-month rating, 3 patients had a fresh episode. At the 6-month rating, there were 2 such patients. These were not considered for computing the YMRS and CGAS scores.  
<sup>d</sup>RMANOVA = Repeated Measures Analysis of Variance

Twenty-four subjects (96%) recovered from the index episode within the 6-month study period. The subject who did not recover was not considered in our calculation of the time to recovery and total duration of episode. The median time to recovery was 27 days, ranging from 4 to 111 days; mean time to recovery was 32 days (SD 27). Following intake, the cumulative probability of recovery at weeks 2, 4, 6, 8, 16, and 24 was 24%, 56%, 76%, 80%, 88%, and 96%, respectively.

We used Kaplan–Meier's survival curve (log-rank test) to analyze the effects of onset-age, prior episodes of affective illness, first-episode polarity, index-episode polarity, psychotic symptoms, YMRS and CGAS intake scores, comorbidity, and hospitalization on the time to recovery from, and the total duration of, the index episode. None of these covariates predicted time to recovery. However, those with prior episodes of affective illness had significantly longer index episodes (mean 105 days vs 53 days) (log-rank test:  $\chi^2 = 7.23$ , df 1;  $P = 0.0072$ ).

The severity of manic symptomatology lessened over the course of the study period, and the level of functioning greatly improved (Table 2).

## Discussion

The main findings of our study are the high rate of recovery from the index episode and a significant improvement in global functioning. Another important finding is that those who had past episodes tended to have significantly longer index episodes. The findings of a high recovery rate contrast with those of some recent studies (3,5,6) and some older studies (4), which report low rates of recovery and high rates of chronicity. However, our finding accords with high recovery rates reported in some studies, including a previous study from the same centre (1,2). In our current sample, the mean YMRS score at intake was 39, which was higher than the score of 28 reported in a previous study (12); this indicates that our sample had severe manic symptomatology. There are 3 possible explanations for the better outcome in our sample. First, most of our sample were drug-naïve at intake, unlike samples in previous studies (3,6). Further, our sample was self-referred; used the centre as a first-contact, primary clinical

service; and entered the study relatively early in the episode. It is possible that patients seen in larger referral centres may be suffering from chronic forms of illness and from multiple comorbid conditions, resulting in ascertainment bias (13). It is also possible that patients in whom early intervention is carried out tend to have a better prognosis. Second, the low comorbidity rate (36%) could have contributed to the high recovery rate. Comorbid ADHD has been reported to be associated with poor recovery (3). In our sample, ADHD was comorbid in only 4%, which is very low, compared with the high rates reported previously (12,14,15). Comorbid conduct disorder and comorbid oppositional defiant disorder were present in 4% and 28%, respectively. This was similar to comorbidity reported in a previous study (12) and much lower than that reported in other studies (11,14,15). Third, our sample consisted mainly of adolescents, whereas other studies included a predominantly prepubertal population (3,6,15). That adolescents may have better recovery rates is further supported by the findings of other studies with predominantly adolescent samples (1,2). Finally, whether these findings reflect true cross-cultural differences in the outcome of juvenile BD needs further exploration.

The findings of our study have to be interpreted with certain limitations in mind. The sample size was small and not controlled for medication. In addition, the rater was not blind to the patients' baseline clinical and medication status.

However, the findings of our study have important clinical and research implications. That most of our patients recovered within a short-term period of intensive treatment highlights the importance of aggressive pharmacologic intervention for patients with juvenile BD. The difference in sample characteristics—especially the relatively low rates of comorbidity—and the early institution of treatment may have been a major contributing factor. Second, our findings confirm a previous report from our centre that recovery rates are high (2), which raises the possibility of cross-cultural variation in outcome. This observation has to be understood in the context of favorable prognosis reported for schizophrenia among adults from developing countries, compared with adults from developed countries (16). It is therefore imperative to examine the

course of juvenile BD in larger samples prospectively to confirm whether these variations are truly cross-cultural or the result of different ascertainment methods and sample characteristics.

## References

1. Strober M, Schmidt LS, Freeman R, Bower S, Lampert C, DeAntonio M. Recovery and relapse in adolescents with bipolar affective illness: a five-year naturalistic prospective follow up. *J Am Acad Child Adolesc Psychiatry* 1995;34:724-31.
2. Srinath S, Reddy JYC, Girimaji SR, Seshadri SP, Subbakrishna DK. A prospective study of bipolar disorder in children and adolescents from India. *Acta Psychiatr Scand* 1998;98:437-42.
3. Biederman J, Mick E, Bostic JQ, Prince J, Daly J, Wilens TE, and others. The naturalistic course of pharmacologic treatment of children with manic-like symptoms: a systematic chart review. *J Clin Psychiatry* 1998;59:628-37.
4. De Long GR, Aldershof AL. Long-term experience with lithium treatment in childhood: correlation with clinical diagnosis. *J Am Acad Child Adolesc Psychiatry* 1987;26:389-94.
5. Geller B, Zimmerman B, William M, Bolhofner K, Craney JL, Delbello MP, and others. Six-month stability and outcome of a prepubertal and early onset bipolar disorder phenotype. *J Child Adolesc Psychopharmacol* 2000;10:165-73.
6. Geller B, Craney JL, Bolhofner K, Delbello MP, William M, Zimmerman B. One-year recovery and relapse rates of children with a prepubertal and early onset bipolar disorder phenotype. *Am J Psychiatry* 2001;158:303-5.
7. Srinath S, Bharath S, Girimaji S, Seshadri SP. Characteristics of a child inpatient population with hysteria in India. *J Am Acad Child Adolesc Psychiatry* 1993;32:822-5.
8. Herjanic B, Reich W. Development of a structural interview for children: agreement between parent and child on individual symptoms. *J Abnorm Child Psychol* 1982;10:307-24.
9. Young RC, Biggs JT, Zeigler VE, Meyer DA. A rating scale for mania: reliability, validity and sensitivity. *Br J Psychiatry* 1978;133:429-35.
10. Shaffer D, Gould SM, Brasic J, Bird H, Fisher P. A children's global assessment scale (C-GAS). *Arch Gen Psychiatry* 1983;40:1228-31.
11. Kovacs M, Pollock M. Bipolar disorder and comorbid conduct disorder in childhood and adolescents. *J Am Acad Child Adolesc Psychiatry* 1995;34:715-23.
12. Kafantaris V, Coletti DJ, Dicker R, Padula G, Pollack S. Are childhood psychiatric histories of bipolar adolescents associated with family history, psychosis and response to lithium treatment? *J Affect Disord* 1998;51:153-64.
13. Reddy YCJ, Srinath S. Juvenile bipolar disorder. *Acta Psychiatr Scand* 2000;102:162-70.
14. Wozniak J, Biederman J, Keily K, Ablon S, Faraone S, Mundy E, and others. Mania-like symptoms suggestive of childhood onset bipolar disorder in clinically referred children. *J Am Acad Child Adolesc Psychiatry* 1995;34:867-76.
15. Biederman J, Faraone SV, Chu MP, Wozniak J. Further evidence of a bidirectional overlap between juvenile mania and conduct disorder in children. *J Am Acad Child Adolesc Psychiatry* 1999;38:468-76.
16. Jablensky A. Epidemiology of schizophrenia. In: Gelder GM, Lopes-Ibor JJ, Andreasen N, editors. *The new Oxford textbook of psychiatry*. Oxford University Press; 2000. p 585-99.

Manuscript received March 2002, revised, and accepted October 2002.

<sup>1</sup>Senior Resident, Department of Psychiatry, National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India.

<sup>2</sup>Professor, Department of Psychiatry, National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India.

<sup>3</sup>Associate Professor, Department of Psychiatry, National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India.

<sup>4</sup>Assistant Professor, Department of Psychiatry, National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India.

<sup>5</sup>Additional Professor, Department of Psychiatry, National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India.

<sup>6</sup>Additional Professor, Department of Biostatistics, National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India.

*Address for correspondence:* Dr S Srinath, Department of Psychiatry, PO Box 2900, National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore 560 029, India.  
e-mail: shobas@nimhans.kar.nic.in

### Résumé : L'épisode maniaque de référence marquant l'apparition juvénile du trouble bipolaire : le modèle de rétablissement

**Objectif :** De récentes études menées auprès de patients souffrant du trouble bipolaire juvénile révèlent de faibles taux de rétablissement et des taux élevés de chronicité. Toutefois, il y a absence de données sur les résultats à court terme. Cette étude examine le modèle de rétablissement de l'épisode de référence dans un échantillon juvénile traité énergiquement.

**Méthode :** Nous avons évalué 25 sujets (16 ans) ayant reçu un diagnostic de manie, à l'aide de l'entrevue diagnostique pour enfants et adolescents révisée (DICA-R), de l'échelle de cotation de la manie chez les jeunes (YMRS) et de l'échelle d'évaluation globale des enfants (CGAS) à l'admission et ensuite, à 3 et 6 mois. Nous avons étudié le temps requis pour se rétablir de l'épisode de référence, le niveau de fonctionnement et les facteurs qui les prédisent.

**Résultats :** Après 6 mois, 24 sujets (96 %) s'étaient rétablis de l'épisode maniaque de référence. Le temps moyen de rétablissement était 27 jours. La durée totale de l'épisode était significativement plus longue chez les sujets ayant eu des épisodes affectifs antérieurs.

**Conclusions :** Les résultats indiquent que la manie d'apparition juvénile a des taux élevés de rétablissement et de faibles taux de chronicité. Ces différences par rapport à la documentation existante nécessitent une étude approfondie.