Increased Prospective Health Service Use for Depression among Adults with Childhood Onset Bipolar Disorder

Regina Sala, MD, PhD[1,2,*], Benjamin I. Goldstein, MD, PhD[3], Shuai Wang, PhD[1], Ludwing Flórez-Salamanca, MD[1], Miren Iza, MD[1], and Carlos Blanco, MD, PhD[1]

Objective To examine the prospective relationship between age of onset of bipolar disorder and the demographic and clinical characteristics, treatment, new onset of psychiatric comorbidity, and psychosocial functioning among adults with bipolar disorder.

Study design As part of the National Epidemiologic Survey on Alcohol and Related Conditions, 1600 adults who met lifetime *Statistical Manual of Mental Disorders, 4th edition* criteria for bipolar disorder-I (n = 1172) and bipolar disorder-II (n = 428) were included. Individuals were evaluated using the *Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV* version for *Diagnostic and Statistical Manual of Mental Disorders, 4th edition,* and data were analyzed from Waves 1 and 2, approximately 3 years apart. Individuals with bipolar disorder were divided into three age at onset groups: childhood (<13 years old, n = 115), adolescence (13-18 years old, n = 396), and adulthood (>19 year old, n = 1017).

Results After adjusting for confounding factors, adults with childhood-onset bipolar disorder were more likely to see a counselor, have been hospitalized, and have received emergency room treatment for depression compared with those with adulthood-onset bipolar disorder. By contrast, there were no differences in the severity of mania or hypomania, new onset of comorbidity, and psychosocial functioning by age of bipolar disorder onset.

Conclusions Childhood-onset bipolar disorder is prospectively associated with seeking treatment for depression, an important proxy for depressive severity. Longitudinal studies are needed in order to determine whether prompt identification, accurate diagnosis, and early intervention can serve to mitigate the burden of childhood onset on the long-term depressive burden of bipolar disorder. *(J Pediatr 2013;163:1454-7).*

The onset of bipolar disorder in childhood and adolescence is increasingly recognized to be associated with greater illness severity, poorer outcome,[1-3] and serious disruption of the development and emotional growth of the youth.[4] Compared with adult-onset bipolar disorder, childhood- and adolescent-onset bipolar disorder have been associated with more episodes and greater severity of mania and depression, earlier recurrence of mood episodes after initial remission, ultradian cycling, fewer days of euthymia, greater delays to first treatment contact, more comorbidities and suicide attempts, greater impairment in functioning and quality of life, and higher health care costs.[1,5-9]

Most of the studies that have compared the age at onset of bipolar disorder have relied on clinical samples, the results of which may not generalize to the broader population of individuals with bipolar disorder. To our knowledge, there are no published prospective epidemiologic studies examining the course of bipolar disorder by age at onset of bipolar disorder. Given the clinical relevance and potential prognostic implications of childhood-onset bipolar disorder, we sought to build on prior cross-sectional work,[10] by drawing on the longitudinal design of the National Epidemiologic Survey on Alcohol and Related Conditions (NE-SARC) to examine the course of bipolar disorder-I (1 or more manic or mixed episodes; severe impairing) and bipolar disorder-II (at least 1 hypomanic episode; less severe) by age at onset of bipolar disorder. We hypothesized that, compared with individuals with adult-onset bipolar disorder, adults with childhood-onset bipolar disorder would have: (1) greater number and length of hypomanic/manic and depressive episodes and lower rates of recovery from both; (2) higher rates of treatment seeking for hypomania/mania and depression; and (3) higher incidence of psychiatric comorbidity and lower psychosocial functioning.

Methods

The NESARC[11,12] is a longitudinal nationally representative survey based on the civilian non-institutionalized population of the US, age 18 years old and over.

AUDADIS-IV	*Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV*
DSM-IV	*Diagnostic and Statistical Manual of Mental Disorders, 4th edition*
NESARC	National Epidemiologic Survey on Alcohol and Related Conditions

Data collection was conducted in two waves using face-to-face interviews. Wave 1 interviews (n = 43 093) were conducted between 2001 and 2002 by trained lay interviewers who had an average of 5 years of experience working on census and other health-related national surveys.[11] The current study utilized data from Wave 1 as well as Wave 2 interviews, which were conducted between 2004 and 2005 with 34 653 of the NESARC Wave 2 respondents.[12] After accounting for those ineligible for the Wave 2 interview (eg, deceased), the response rate for Wave 2 was 86.7%. The mean interval between Wave 1 and Wave 2 interviews was 36.6 (SD = 2.62) months. The research protocol, including informed consent procedures, received full human subjects review and approval from the US Census Bureau and the US Office of Management and Budget. Institutional Review Board approval was obtained prior to participant enrollment. Informed consent was obtained from all participants before beginning the interviews. Detailed descriptions of methodology, sampling, and weighting procedures can be found elsewhere.[11]

The number of participants included in the present study (n = 1598) were those with lifetime diagnosis of bipolar disorder-I (n = 1172) and bipolar disorder-II (n = 426) in Wave 1 based on age of onset of mania or hypomania. By contrast, in our prior cross-sectional study,[10] we included only those participants with lifetime diagnosis of bipolar disorder-I (n = 1411) based on age of onset of mania to determine bipolar disorder onset age. To be consistent with previous studies,[6,10] respondents with lifetime diagnosis of bipolar disorder-I and bipolar disorder-II (n = 428) in Wave 1 were divided into three groups: childhood (<13 years old, 8.92% n = 115), adolescence (13-18 years old, 28.14%, n = 396), and adulthood (>19 years old, 62.94%, n = 1017).

Sociodemographic measures included age, sex, race/ethnicity, marital status, education, employment status and personal income.

All diagnoses were made according to *Diagnostic and Statistical Manual of Mental Disorders, 4th edition* (DSM-IV) criteria using the Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV) version for DSM-IV, a valid, reliable, fully structured diagnostic interview designed for use by professional interviewers who are not clinicians.[13] Reliability is fair for the bipolar disorder-I diagnosis (κ = 0.59), good for bipolar disorder-II (κ = 0.69),[14] and is excellent for alcohol diagnoses ($\kappa \geq 0.74$) and drug diagnoses ($\kappa \geq 0.79$).[15] The anxiety disorders included in the present study are social anxiety disorder, panic disorder, and generalized anxiety disorder, which have fair to good reliability (κ = 0.42-0.52).[15]

Based on the findings of previous studies, we compared the following by age at onset of bipolar disorder: (1) demographic characteristics; (2) clinical characteristics of bipolar disorder, including course of symptoms and treatment utilization between Wave 1 and Wave 2; (3) incidence of psychiatric comorbidities between Wave 1 and Wave 2; and (4) psychosocial functioning at Wave 2, as assessed by the mental health, social functioning, and role emotional subscales, as well as the mental component summary of the 12-item *Short Form Health Survey, version 2*, a reliable and valid measure of disability used in population surveys.[16]

Statistical Analyses

Weighted percentages and means were computed to derive associations with prospectively ascertained comorbidities, treatment, and level of functioning among respondents with bipolar disorder by age at onset. To be consistent with our prior research,[10] we used the 6-month cut-off point for the duration of the episodes. Because the combined SE of 2 means or percentages is always equal to or less than the sum of the SEs of those 2 means, we conservatively consider that 2 CIs that do not overlap to be significantly different from one another.[17] Multinomial logistic regression was used to obtain aOR for new onset of comorbidities, functioning, clinical characteristics of bipolar disorder, and treatment for bipolar disorder adjusted for age, sex, race, and income. Multiple linear regression was used to obtain adjusted means for continuous variables. All P values are based on two-tailed tests with $\alpha = 0.05$. All analyses, including parameter estimates, SEs, and 95% CI were performed using SUDAAN (RTI International, Research Triangle Park, North Carolina), a statistical software package that adjusts for the design effect of complex sample surveys like the NESARC.

Results

Compared with adult-onset bipolar disorder, childhood- and adolescent-onset bipolar disorder were associated with lower odds of being female and of being married or cohabiting (Table I; available at www.jpeds.com). In addition, compared with adult-onset bipolar disorder, childhood-onset bipolar disorder was associated with lower odds of being Hispanic and of having higher education, whereas adolescent-onset bipolar disorder was associated with lower personal income and lower odds of family history of alcohol abuse or dependence.

Childhood- and adolescent-onset of bipolar disorder were associated with lower age of onset of depression and more mania onset first than depression compared with those with adult-onset bipolar disorder (Table II; available at www.jpeds.com).

Compared with adult-onset of bipolar disorder, childhood-onset of bipolar disorder was associated with greater odds of having received any treatment for depression between Waves 1 and 2, including seeing a counselor, having been hospitalized for depression, and having sought emergency room treatment. By contrast, there were no differences in the probability or type of treatment between individuals with adolescent- vs adult-onset bipolar disorder. In addition, there were no differences in the clinical characteristics of bipolar disorder or in the treatment for mania or hypomania among individuals by age at onset of bipolar disorder (Table II).

In addition, a subanalysis of the clinical characteristics and treatment for depression at Wave 1 found that compared