Medical Comorbidity Among Youth Diagnosed With Bipolar Disorder in the United States

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Objective: This study examines the number and type of medical comorbidities among youth diagnosed with bipolar disorder.

Method: This is a retrospective data analysis using the 2000–2001 Thomson Medstat MarketScan medical claims and administrative files. The population included a national sample of youth (ages 6–18 years) from privately insured families within the United States. Number of chronic medical conditions and type of medical comorbidity were analyzed in *ICD-10*–diagnosed youth with bipolar disorder (N = 832) and other types of psychiatric disorders (N = 21,493) using The Johns Hopkins Adjusted Clinical Groups Case Mix System, Version 8.0.

Results: Thirty-six percent of youth with bipolar disorder had 2 or more chronic health conditions versus 8% of youth with other psychiatric diagnoses. The following categories of medical conditions were significantly more prevalent in youth diagnosed with bipolar disorder: cardiology, gastrointestinal/hepatic, neurologic, musculoskeletal, female reproductive, and respiratory. Toxic effects and adverse events were also higher in youth with bipolar disorder, compared to youth with other psychiatric disorders.

Conclusions: Youth with bipolar disorder experience higher rates of several medical illnesses compared to youth with other psychiatric diagnoses. Several factors may explain this phenomenon, including worse medication side effects, unhealthy lifestyle behaviors, poorer access to health care services, socioeconomic status, and biologic susceptibility. Moreover, a diagnosis of bipolar disorder may reflect more frequent health care utilization and therefore more opportunities for additional medical diagnoses. Further understanding regarding reasons for these relatively high rates of comorbidity among youth diagnosed with bipolar disorder may be helpful in improving overall health and quality of life during the early stages/onset of this disorder.

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Early onset bipolar disorder is a serious and debilitating illness, as evidenced by high rates of morbidity and mortality, accompanied by increased levels of health service utilization. Severity of psychiatric illness is likely a large factor influencing outcomes; however, additional chronic medical conditions may contribute to the poor outcomes of these youth as well. It has been shown that adults with bipolar disorder are likely to have high rates of chronic medical illnesses, especially migraine headaches, cardiovascular, cerebrovascular, pulmonary, respiratory, and gastrointestinal conditions.[1–4]

A high prevalence of medical comorbidity significantly impacts overall health. Research has demonstrated the significance of comorbidities in terms of health care utilization and economic consequences. In adolescents with asthma and comorbid depressive disorders, health care costs may be influenced to a greater extent by presence of comorbidity than by illness severity alone.[5] Additionally, Kelleher and Starfield[6] showed that in children with mental health–related diagnoses, the number of medical comorbidities was the most powerful predictor for primary care and total health care utilization.

Although information on the rates of medical comorbidity in adults with bipolar disorder has been well established, the idea that youth with bipolar disorder may have increased rates of medical conditions is not addressed in the literature. Looking at a more comprehensive picture of these children and their health care needs might offer us insight into the best way to organize services for these children. Therefore, this article examines number of and type of medical comorbidities among youth with bipolar disorder.

METHOD

Data Source

The data are from the Thomson Medstat MarketScan (2000–2001) database, a national dataset containing standardized, detailed, enrollee-specific clinical utilization

information across inpatient and outpatient services and prescription drug information from approximately 45 employer-sponsored health plans covering all regions of the country; therefore, youth in this study represent minors from employed families. This project was approved by the Johns Hopkins University Bloomberg School of Public Health institutional review board. Because this was de-identified, secondary data, informed consent was waived by the review board.

Sample Characteristics

Behavioral health claims from an incident cohort (N = 832) of privately insured youth 6–18 years of age who had at least 2 outpatient or 1 inpatient claim associated with a bipolar disorder diagnosis were examined and compared to claims of youth with other psychiatric diagnoses of the same age (N = 21,493). Youth with no psychiatric diagnoses were excluded from the study. Lurie and colleagues[7] evaluated the accuracy of schizophrenia diagnoses in claims data using these same criteria and reported a high positive predictive value (94%), although sensitivity was more modest (80%). The validity of using a claims dataset and the approach described by Lurie et al has been explored for other mental health diagnoses in adults, such as bipolar disorder, schizophrenia, and depression,[8–10] where diagnoses were found to be accurate between 75%–95% of the time when compared to evaluation of medical records. This method has also been shown to accurately distinguish between diagnoses of bipolar disorder and schizophrenia.[8]

Only youth having complete coverage for the 2-year period were included to ensure they had the opportunity to access all types of care, addressing other factors such as copayment or distance to facilities, which may vary among individuals. Analysis comparing amount of time continuously enrolled showed that youth with 2 years of continuous enrollment are likely to differ from those insured for shorter periods of time. Indeed, compared with youth enrolled for 1 year or less, those with 2 years of continuous enrollment were more likely to be in a health maintenance organization and less likely to be in a point of service plan. Also, those with 2 years of continuous enrollment were significantly more likely to live in the Northeast and less likely to live in the West. There were, however, no age or gender differences between these groups. So, although this is not a probabilistically representative sample of the entire nation, it is a large sample of youth from all regions of the country enrolled during 2000 and 2001 in all types of private health insurance plans.

Availability of Physicians

Data on the availability of physicians in each county were used as an indicator of the regional accessibility of health care services using data from the 2001 Area Resource File (ARF).[11] This file provides statistics at the county level on the supply and/or availability of physicians. The ARF data on the availability of physicians were linked to the claims data using the county of residence for each youth. The total number of physicians in the youth's county of residence was divided by the number of youth 6–18 years old living in the county to construct this variable.

Diagnostic Categories

The Johns Hopkins Adjusted Clinical Groups (ACG) Case Mix System, Version 8.0, was used to characterize type of medical comorbidity and categorize diagnoses received.[12] Development and validation of the ACG system have been performed in the United States, and it is frequently used in studies addressing medical comorbidity and/or overall medical disease burden.[13–15]

Specifically, major expanded diagnostic clusters (MEDCs; ie, broad clinical categories) were used to classify each medical diagnosis received by individuals. All *ICD-10* codes are translated to 1 of 264 expanded diagnostic clusters (EDCs) that are then condensed into 1 of 27 MEDC codes.[12] In order to ensure a sufficiently large sample for analysis, the most common MEDC codes (those having a prevalence of at least 10%) were examined. *ICD-10* coding is primarily used in US practices and is all that is available in administrative data. Prior studies have shown a rather high concordance between *ICD-10* and *DSM-IV* on several mental health conditions among adolescents.[16,17]

Chronic Medical Conditions

Health conditions derived from EDCs include an indicator for those defined as chronic conditions (ie, conditions expected to require long-term management for longer than 1 year). The number of EDCs categorized as chronic conditions are subsequently tabulated for each individual. Chronic conditions that were categorized as psychosocial (ie, mental health– and/or substance abuse–related diagnoses) were excluded from the overall count.

Resource Utilization Band

Resource utilization bands (RUBs) were calculated for each individual to provide an additional indicator of comorbidity. RUB categories are based on a combination of clinical criteria, age, and gender and group individuals based on expected future resource use. The RUB indicator ranges from 0 (no resource users) to 5 (high resource users). These categories have been empirically validated to support the assumption that people with greater comorbidity are likely to use more medical care resources, and the RUB indicator has also been used to approximate the severity of an enrollee's comorbidity.

Psychiatric Diagnoses

International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes 290 through 319 were used to define mental disorders. All *ICD-9-CM* diagnoses between 295 and 319, inclusive, were included

Table 1. Sample Characteristics for Youth Diagnosed With Bipolar Disorder Versus Youth With Any Other Behavioral Health Disorder

Patient Characteristic	Youth Diagnosed With Bipolar Disorder (N = 832), % (95% CI)	Youth Diagnosed With Other Behavioral Health Disorders (N = 21,493), % (95% CI)
Age		
6–11 y	13.5 (10.6–16.2)*	33.8 (33.2–34.4)
12–14 y	24.6 (21.8–27.7)	21.9 (21.4–22.5)
15–16 y	30.5 (27.4–33.8)*	18.6 (18.1–18.2)
17–18 y	31.4 (28.3–34.7)*	25.7 (25.1–26.2)
Sex, male	55.2 (51.5–58.4)	57.7 (57.0–58.3)
Managed care		
Fee for service	29.7 (26.6–32.9)*	34.3 (33.7–34.9)
Managed care	70.3 (67.1–73.4)*	65.7 (65.1–66.3)
Urbanicity, urban	88.1 (85.7–90.2)	87.7 (87.2–88.1)
RUB (comorbidity) category		
Low	48.4 (45.0–51.9)*	82.5 (82.0–83.0)
Medium	39.4 (36.1–42.8)*	14.9 (14.4–15.4)
High	12.1 (10.0–14.6)*	2.6 (2.4–2.9)
Psychiatric diagnoses		
Bipolar disorder	100.0	—
Depression	63.5 (60.1–66.8)*	31.0 (30.4–31.6)
ADHD	33.0 (29.8–36.3)*	39.7 (39.0–40.4)
ODD/CD	24.7 (21.8–27.8)*	8.2 (7.8–8.6)
Anxiety	14.0 (11.8–16.6)	12.6 (12.2–13.1)
Schizophrenia	4.9 (1.7–8.3)*	0.3 (0.1–0.7)

*Significant at the $P = .05$ level.
Abbreviations: ADHD = attention-deficit/hyperactivity disorder, CD = conduct disorder, ODD = oppositional defiant disorder, RUB = resource utilization band.

(individuals with a diagnosis of organic psychotic conditions, ie, *ICD-9-CM* codes 290–294, were excluded). Diagnoses received were grouped into 6 categories: bipolar disorder (296.0–296.1; 296.4–296.8), attention-deficit/hyperactivity disorder (314), anxiety disorders (300.0; 300.2–300.3; 301; 309.21; 313.0), conduct-related disorders (312 and 313), depression (296.2–296.3; 300.4; 309.0; 311), schizophrenia (295), and other disorders (the most prevalent psychiatric diagnoses received by the cohort of youth diagnosed with bipolar disorder, ie, those with a prevalence of at least 5%, were categorized separately from "other"). The prevalence of all psychiatric diagnoses made over the 2-year enrollment period was calculated for youth diagnosed with bipolar disorder and for youth in the control cohort (ie, all other diagnoses per above).

Statistical Analyses

Descriptive statistics were calculated for demographic, clinical, and insurance plan characteristics for youth diagnosed with bipolar disorder compared to youth diagnosed with other psychiatric disorders. Estimates and confidence intervals were computed to better characterize the precision of the estimates and the magnitude of differences between groups.

Multivariable logistic regression determined the odds of receiving a diagnosis from each of the 9 specific medical diagnostic categories (yes/no) in youth diagnosed with bipolar disorder compared to youth diagnosed with other psychiatric diagnoses. For each odds ratio, 95% confidence intervals were also computed. Independent variables entered were age, gender, type of insurance, and availability of physicians. Statistical analyses were carried out using SAS 9.1 (SAS Institute Inc, Cary, North Carolina).

RESULTS

Sample Characteristics

Youth diagnosed with bipolar disorder had a mean age of 14.7 years. About half of these youth were male (55%), with the majority living in an urban/suburban area (88%). These individuals were significantly more likely to be older, be enrolled in a managed care plan, and have higher RUB scores compared to youth with other psychiatric disorders (Table 1).

Chronic Medical Conditions

The majority (73%) of youth diagnosed with bipolar disorder were being treated for chronic medical conditions. For these patients, the number of chronic medical conditions ranged from 1 to 7. Youth diagnosed with bipolar disorder were more likely to have multiple chronic medical conditions compared to youth diagnosed with other psychiatric disorders as 36% of youth diagnosed with bipolar disorder had 2 or more chronic medical conditions compared to 8% of youth with other psychiatric diagnoses.

Types of Chronic Medical Conditions

More than half of youth diagnosed with bipolar disorder also received a diagnosis of a chronic medical condition categorized as a chronic ear, nose, throat disorder (57.8%) or a musculoskeletal disorder (53.5%), and at least one-third of youth received a diagnosis categorized as a chronic respiratory disorder (45.0%) or neurologic disorder (34.6%). The control group showed medical comorbidity as well, though to a lesser extent. Among the control group of youth diagnosed with other psychiatric disorders, more than half received a diagnosis categorized as a chronic ear, nose, throat condition (64.4%) and more than one-third received a diagnosis of a chronic musculoskeletal (45.3%) or respiratory (40.4%) disorder. One-quarter (25.4%) received a diagnosis of a neurologic disorder (Table 2).

In the multivariable models (Table 3), when adjusting for additional covariates, including age, gender, and availability of physicians, the following types of medical conditions were significantly more prevalent in youth diagnosed with bipolar disorder: cardiology (OR = 1.95; 95% CI, 1.59–2.38), gastrointestinal/hepatic (OR = 1.46; 95% CI, 1.23–1.72), neurologic (OR = 1.55; 95% CI, 1.34–1.80), musculoskeletal (OR = 1.21; 95% CI, 1.05–1.39), female reproductive

Table 2. Prevalence of Types of Specialty Diagnoses Made in Youth With Bipolar Disorder Versus Youth With Other Behavioral Health Disorders

Type of Specialty	Prevalence in Youth With Bipolar Disorder (N = 832), % (95% CI)	Prevalence in Youth With Other Behavioral Health Disorders (N = 21,493), % (95% CI)
Cardiology	14.2 (12.0–16.7)*	7.1 (6.8–7.5)
Ear, nose, throat	57.8 (54.5–61.0)	64.4 (63.8–65.0)
Endocrine	10.0 (8.1–12.2)*	5.2 (4.9–5.5)
Gastrointestinal/hepatic	21.0 (18.4–24.0)*	15.1 (14.6–15.6)
Neurologic	34.6 (31.5–37.9)*	25.4 (24.8–26.0)
Musculoskeletal	53.5 (50.1–56.9)*	45.3 (44.8–45.7)
Female reproductive	21.0 (18.3–23.8)*	11.5 (11.1–12.0)
Respiratory	45.0 (41.6–48.4)*	40.4 (39.5–40.9)
Toxic effects and adverse events	15.1 (12.9–17.7)*	4.4 (4.1–4.7)
Multiple comorbidities		
2 or more	36.2 (33.0–40.0)*	8.0 (6.4–10.1)
3 or more	15.0 (14.5–15.5)*	2.8 (2.6–3.1)

*Significant at the $P = .05$ level.

Table 3. Odds Ratios of Receiving Specialty Diagnoses in Youth With Bipolar Disorder Relative to Youth With All Other Behavioral Health Disorders

Type of Specialty	Odds Ratio (95% CI)[a]
Cardiology	1.95 (1.59–2.38)
Ear, nose, throat	0.30 (0.09–0.97)*
Endocrine	1.04 (0.14–8.0)
Gastrointestinal/hepatic	1.46 (1.23–1.72)*
Neurologic	1.55 (1.34–1.80)*
Musculoskeletal	1.21 (1.05–1.39)*
Female reproductive	1.94 (1.56–2.41)*
Respiratory	1.24 (1.08–1.42)*
Toxic effects and adverse events	3.45 (2.82–4.21)*

[a]These models were adjusted for additional covariates including age, sex, type of insurance, and availability of physicians.
*Significant at the $P = .05$ level.

(OR = 1.94; 95% CI, 1.56–2.41), and respiratory (OR = 1.24; 95% CI, 1.08–1.42). Toxic effects and adverse events (this included toxic effects from nonmedicinal agents and adverse effects due to medicinal agents and complications due to medical surgery or mechanical devices) were also higher in youth diagnosed with bipolar disorder compared to youth with other psychiatric disorders (OR = 3.45; 95% CI, 2.82–4.21). Conversely, any ear, nose, throat diagnosis was more prevalent in youth with other psychiatric disorders compared to youth diagnosed with bipolar disorder (OR = 0.30; 95% CI, 0.09–0.97).

DISCUSSION

In this study, we examined medical comorbidity in youth 6–18 years old diagnosed with bipolar disorder. We demonstrated that the majority of youth diagnosed with bipolar disorder are being treated for other chronic medical conditions, a significantly greater number than a group of youth with other psychiatric diagnoses. In addition, youth diagnosed with bipolar disorder also have elevated rates of medical disorders in certain specialty areas compared to youth diagnosed with other psychiatric diagnoses. Several factors may explain poorer overall health, including worse medication side effects, unhealthy lifestyle behaviors, poorer access to health care services, socioeconomic status differences, and biologic susceptibility. For example, research suggests that activated inflammatory response systems and dysfunction among other intracellular processes may be associated with bipolar disorder and may contribute to system-wide susceptibility of other disease processes.[18] Moreover, the diagnosis of bipolar disorder may reflect timely health care and therefore more opportunities for greater medical diagnoses.

Although there is not evidence in the literature to support that all of the medical conditions described in this article are caused by medications, there is emerging evidence that the medications used for mood stabilization, in particular, the atypical antipsychotics, have the potential for cardiac,[19] metabolic, and endocrine side effects.[20–22] However, a recent study displayed that numerous factors, in addition to medications, can lead to obesity in bipolar youths.[23] It is also unclear how much of this relationship is bidirectional (ie, Do patients with bipolar disorder have premorbid risk for medical complications, are they more susceptible to the side effects of medications, or is there a combination of intrinsic and external factors?).[24] This topic is of added importance as the use of these medications in children and adolescents has increased over the past decade.[25] Clearly, a cross-sectional study such as ours cannot answer these questions, but our study highlights the need for caution in prescribing, the need for careful monitoring of medical conditions, and the need for longitudinal studies with this population.

Previous research indicates that youth diagnosed with bipolar disorder have higher behavioral health care costs and behavioral health care utilization rates compared to youth with other mood or nonmood behavioral health disorders.[26] Additionally, it has been shown that youth with bipolar disorder often have high rates of psychiatric comorbidity.[27,28] This study, however, suggests that other chronic medical conditions may also significantly impact the health of these youth and may attribute directly to prior findings of greater health care utilization and cost. While studies have shown significant medical comorbidity among adults with bipolar disorder, this study represents a novel observation pertaining to medical comorbidity in youth.

There is little known about how medical comorbidity in patients with bipolar disorder is evaluated and treated in specialty care.[29,30] Data from the Veterans Health Administration, the nation's largest integrated health care system, reveal challenges to providing access and appropriate medical care to adults with bipolar disorder.[31] Zeber et

al[31] showed that these individuals perceived far more difficulty in getting medical services compared to psychiatric care, suggesting that appropriately coordinated care can be fragmented even within putatively fully integrated systems. Initiatives for the development of care systems to address the complex needs of adults with bipolar disorder are being developed and tested,[32,33] with promising results offering potential improvements in overall care for vulnerable patients with multiple medical and mental health disorders. Children with bipolar disorder, however, are also likely to have complex problems and have unique service needs that may go unrecognized in specialty mental health services. It has been suggested that even in children, medical care often narrowly focuses on diseases rather than implementing a broader view including "various aspects of health and their interactions."[30] This seems important to address early on. Health care utilization patterns develop early on and as youth with bipolar disorder transition into young adulthood, the complexity of caring for their multiple comorbidities promises to remain a substantial challenge for many health care systems.

These data need to be interpreted with caution. Although epidemiologic studies using the *DSM-IV* criteria find that only approximately 1% of children and adolescents meet full criteria for bipolar disorder,[34,35] the last decade has witnessed a 4-fold increase in adolescents who are discharged from psychiatric hospitals carrying a diagnosis of bipolar disorder[36] and a 40-fold increase in office visits of youth with this diagnosis.[37] In addition to changes in physician practice style, issues such as misdiagnoses, "up-coding" for reimbursement, or increased awareness may contribute to increased rates of bipolar disorder diagnoses in utilization data. However, these findings are important and generalizable to youth with a diagnosis of bipolar disorder in current health care settings. In addition, youth diagnosed with bipolar disorder are a heterogeneous group, and the claims dataset provides a limited picture of their clinical characteristics. Although it is possible that comorbidity may differ between bipolar disorder subtypes, claims data do not reliably distinguish between these groups.

Given the relative rarity of the disorder and the limited generalizability of small clinical studies, however, administrative data on diagnosis and service utilization among large community samples can be an important source of information. These data serve as a starting point for more definitive studies. At this point, we provide potential diagnostic patterns of a substantial number of youth in a community setting who have received a diagnosis of bipolar disorder.

Future studies should specifically examine the association between mental health and multiple physical diagnoses with longitudinal patterns of health services use, cost, clinical outcomes, and overall quality of life. Additionally, temporal relationship of disorder onset (eg, timing of bipolar disorder in relation to onset of medical disorders and in relation to psychotropic medication use) should be further explored. Results also suggest need for services research around developing a model of care that more specifically addresses the needs of children and adolescents with bipolar disorder. A recent report[38] has documented the severe medical needs and difficulty in accessing services specific to the needs of young adults with bipolar disorder; so, as children and adolescents transition into adulthood, we must recognize the panoply of health needs they already face and will continue to experience.[5] Accessing services specific to their needs and maintaining continuous care with multiple fragmented programs will be especially challenging. Health service planning and physician training around the management of these complex individuals must incorporate a balance of mental health and physical illnesses. Mental health clinicians may need additional training around the medical needs of these youth. Additionally, given the substantial medical needs of some youth with bipolar disorder, health care systems may need to be improved to facilitate access to and continuity of both medical and mental health care for these youth. Further research into these areas and understanding reasons for these relatively high rates of comorbidity among youth with bipolar disorder in addition to the specific conditions that are more prevalent will be helpful in improving overall health and quality of life of youth with this disorder.

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