Phenomenology and Psychiatric Comorbidity in Pediatric Bipolar Disorder

Pediyatrik Bipolar Bozuklukta Fenomenolojik Özellikler ve Psikiyatrik Komorbidite

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Abstract

Aim: We aimed to investigate phenomenology and psychiatric comorbidity in a clinical sample of young patients with bipolar disorder (BD).

Materials and Methods: Young patients who had been followed up after diagnosis with BD in a faculty clinic were included in the study. Data regarding phenomenology and clinical characteristics of mood episodes were gathered from medical records of the subjects, clinical interviews with the subjects and parents, and the follow-up data of the subjects. Psychiatric assessment was conducted by using a semi-structured diagnostic instrument.

Results: Nineteen males (63%) and eleven females (37%) who were aged between 11 and 18 years (14.87±1.94 years) were included in the study. Their primary diagnoses were BD type I (n=22; 73%), BD type II (n=3; 10%), and BD–Not Otherwise Specified (n=5; 17%). More than half of the subjects (53%) had developed psychotic symptoms (i.e. perceptual and/or thought disturbances) during mood episodes. Nine subjects (30%) had attempted suicide once or twice. The frequency of diagnostic categories from which criteria for at least one disorder met was as follows: anxiety disorders (n=28; 93%), attention deficit hyperactivity disorder (n=23; 77%), depressive disorders (n=16; 53%), tic disorders (n=15; 50%), oppositional defiant disorder (n=8; 27%), and substance use disorders (n=7; 23%)

Discussion and Conclusion: Compared to the adult form of the illness, some developmental differences may be observed in pediatric BD. BD in young subjects is highly comorbid with other psychiatric disorders, particularly anxiety, depressive disorders, and attention deficit hyperactivity disorder. Young subjects with BD should carefully be assessed for comorbid psychiatric disorders for differential diagnosis and treatment planning.

Keywords: bipolar; mood; children; adolescents; phenomenology; comorbidity

Özet

Amaç: Bipolar bozukluğu (BB) olan çocuk ve ergenlerden oluşan bir klinik örneklemde fenomenolojik özellikleri ve psikiyatrik komorbiditeyi araştırmak amaçlanmıştır.

Gereç ve Yöntemler: Bir fakülte hastanesi kliniğinde BB tanısıyla takip edilen çocuk ve ergenler çalışmaya dahil edilmiştir. Duygudurum episodlarına ait fenomenolojik ve klinik özellikler, hasta dosyalarının incelenmesi, hasta ve ailelerle yapılan görüşmeler ve klinik takiplerden elde edilen bilgilerden derlenmiştir. Psikiyatrik değerlendirme aracı olarak yarı yapılandırılmış bir tanısal görüşme formu kullanılmıştır.

Bulgular: Yaşları 11 ile 18 arasında değişen (14.87±1.94 yaş) 19 erkek (%63) ve 11 kadın (%37) hasta çalışmaya dahil edildi. Birincil tanıları BB tip I (n=22; %73), BB tip II (n=3; %10) ve başkatürlü-adlandırılamayan BB (n=5; %17) şeklindeydi. Olguların yarısından fazlasında (%53) psikotik semptomlar vardı. Dokuz olguda (%30) bir veya iki kez intihar girişimi öyküsü vardı. En az bir bozukluk için tanı kriterlerinin karşılandığı komorbid bozukluk tanı gruplarının sıklığı şöyleydi: anksiyete bozuklukları (n=28; %93), dikkat eksikliği hiperaktivite bozukluğu (n=23; 77%), depresif bozukluklar (n=16; %53), tik bozuklukları (n=15; %50), karşı olma karşı gelme bozukluğu (n=8; %27) ve madde kullanım bozuklukları (n=7; %23).

Tartışma ve Sonuç: Pediyatrik BB'de hastalığın erişkin formuna kıyasla bazı gelişimsel farklılıklar görülebilir. Pediyatrik BB özellikle anksiyete, depresif bozukluklar ve dikkat eksikliği hiperaktivite bozukluğu olmak üzere diğer psikiyatrik bozukluklarla yüksek komorbidite göstermektedir. BB'li çocuk ve ergenler ayrıcı tanı ve tedavinin planlanışı açısından psikiyatrik komorbidite için ayrıntılı bir şekilde değerlendirilmelidir.

Anahtar Sözcükler: bipolar; duygudurum; çocuklar; ergenler; klinik özellikler; komorbidite

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INTRODUCTION

Bipolar disorder (BD) is a severe and relatively frequent mood disorder affecting both young and adult populations (1,2). While BD was first described more than one century ago in adults, there has been increasing recognition of BD among young population in the psychiatric literature during the last few decades (3,4). Retrospective studies with adult patients with BD have shown that mood disorder symptoms emerged before 20 years of age in 60%, and before 10 years of age in 10–20% of the subjects (3–7). Studies on the epidemiology of pediatric BD have reported prevalence rates of 1 to 2% and up to 6% when subsyndromal cases included (1–4). Diagnosis of BD in young subjects is made by using the same Diagnostic and Statistical Manual of Mental Disorders (4th edition) Text Revision (DSM-IV-TR) criteria used for adult population (3–5). However, it has been reported that pediatric bipolar disorder (PBD) may have several different aspects, including phenomenology and comorbidity compared to the adult form of the disorder (3–12), and the symptoms vary by age and developmental stage (3,4).

The National Institute of Mental Health Research Group on pediatric BD first suggested in 2001 that pediatric BD can present as "narrow" or "broad" phenotypes (11). Few years later Leibenluft et al. introduced "narrow," "intermediate," and "broad" phenotypes (12). The narrow phenotype is attributed to those that meet the full DSM-IV diagnostic criteria for mania or hypomania, including the duration criterion of 7 and 4 days, respectively, and have the hallmark symptoms of elevated mood or grandiosity. The intermediate phenotypes include two subcategories: those with hallmark symptoms of short duration, i.e., 1–3 days, and those with episodic irritable mania or hypomania meeting the duration criteria without elation. The broad phenotype consists of severe irritability and impulsivity, mood lability, and severe temper outbursts with or without episodicity and without the hallmark symptoms of elated mood or grandiosity. The BD–Not Otherwise Specified (BD-NOS) category in DSM-IV usually corresponds to the intermediate and broad phenotypes. Despite having the classic symptoms of mania or hypomania, a great proportion of young subjects may fail to meet the duration criteria of 4–7 days required to fulfill the DSM-IV criteria for hypomania or mania criteria, respectively, and are usually diagnosed as BD-NOS (3,4).

There is almost a clinical consensus that PBD initially manifests with mixed episodes/features more frequently than in adults (3,4,13–15). Furthermore, nearly half of the adult or young subjects with a diagnosis of BD have reported depressive episodes before their diagnosis of BD (3,4,13–15). Meanwhile, young subjects with BD have been reported to have high rates of psychiatric comorbidity (3,4,16–22). Despite comorbidity rates and patterns may change depending on the age group (children vs adolescents) and setting (clinical vs community samples), high rates of attention deficit hyperactivity disorder (ADHD) (up to 80%), oppositional defiant disorder (ODD) (up to 80%), conduct disorder (CD) (up to 37%), anxiety disorders (AD) (up to 56%), substance use disorders (SUD) (up to 40%), and obsessive compulsive disorder (OCD) (up to 40%) have been reported (16–22). Psychiatric comorbidity has been an important issue in pediatric BD in terms of etiology, phenomenology, differential diagnosis, treatment, and prognosis of the disorder (3,4,16–25).

In this study we aimed to investigate phenomenology and psychiatric comorbidity in a clinical sample of young subjects who had been followed up after a DSM-IV diagnosis of BD in a faculty hospital's child psychiatry clinic.

MATERIALS AND METHODS

Participants

Subjects in this study were recruited from a clinical sample of young subjects who had been followed up after their diagnosis with BD in mood disorder clinic in Child and Adolescent Psychiatry Department at Istanbul Medical Faculty, Istanbul University. The study was conducted between January and July 2009. Subjects who visited the clinic during this period were included in the study. Inclusion criteria were as follows: being aged between 8 to 18 years; having been diagnosed with BD type I, II, or BD-NOS according to DSM-IV criteria; having an IQ level above 55; and consent of the families and assent of the subjects. Exclusion criteria were as follows: having an IQ level below 55; being, and/or having parents who are, unable to conduct

a thorough psychiatric interview for any reason (i.e. acute medical or psychiatric conditions, communication problems); and having been suffering from medication (i.e. antidepressants) induced (hypo)mania.

Instruments

a) Interview Form: This form was developed by the authors in order to investigate and record sociodemographics (i.e. age, gender, education status, family characteristics), medical and developmental history, intellectual level and several illness characteristics (such as age at onset, type, duration, symptoms and number of mood episodes, and suicide attempts during mood episodes).

b) Schedule for Affective Disorders and Schizophrenia for School Age Children–Present and Lifetime Version–Turkish version (K-SADS-PL-T): K-SADS-PL is a widely used semi-structured diagnostic interview that provides a reliable and valid measurement of DSM-IV (American Psychiatric Association, 1994) major psychiatric disorders in children and adolescents (26). The KSADS- PL is administered first to the parent and then to the child, and both parties may be re-interviewed to resolve informant discrepancies. Reliability and validity of Turkish version (K-SADS-PL-T) has been successfully done, showing it is an effective instrument for diagnosing major childhood psychiatric disorders (27).

Procedure

Data regarding bipolar disorder characteristics (i.e. age at onset, type, duration, symptoms and number of mood episodes, hospitalization, suicide attempts during mood episodes) were gathered through reviewing medical records of the subjects as well as clinical interview with the families and subjects. Regarding diagnosis of BD, if a subject had a mood episode with manic symptoms, but failed to meet the duration criteria of 4 or 7 days required to fulfill the DSM-IV criteria for hypomanic or manic episode, he or she was diagnosed as having BD-NOS. Psychometric evaluation had been conducted using Wechsler Intelligence Scale for Children-Revised (WISC-R). All subjects and their parents were interviewed for DSM-IV comorbid psychiatric disorders by using K-SADS-PL. Diagnostic interviews were conducted with subjects and parents in separate

Table 1. Socio-demographic and clinical characteristics of the subjects

Age range	11 to 18 years (14.87±1.94 years)
Gender (males)	n=19; 63.3%
DSM-IV bipolar disorder diagnoses	
BD type I	n=22; 73.3%
BD type II	n=3; 10.0%
BD-NOS	n=5; 16.7%
BD rapid cycling	n=8; 26.7%
First mood episodes (for BD type I or II, n=25)	Age range 11 to 16 years (12.80±2.25 years)
Depressive	n=12; 48.0%
Mixed	n=8; 32.0%
Manic	n=3; 12.0%
Hypomanic	n=2; 8.0%
First bipolar mood episode (for BD type I or II, n=25)	Age range 11 to 16 years (13.24±2.35 years)
Mixed	n=12; 48.0%
Manic	n=10; 40.0%
Hypomanic	n=3; 12.0%
Psychotic symptoms during mood episodes	n=16; 53.3%
Both perceptual and thought disturbance	n=11; 36.7%
Only perceptual disturbance	n=3; 10.0%
Only thought disturbance	n=2; 6.7%
Number of mood episodes	
Less than three episodes	n=14; 46.7%
Between 4 and 10 episodes	n=6; 20.0%
More than 10 episodes	n=10; 33.3%
History of suicide attempts	n=9; 30.0%
Single attempt	n=4; 13.3%
Two times attempt	n=5; 16.7%

Table 2. Symptoms of bipolar mood episodes

Symptoms	n	%
Increased energy or activity level (newly emerged or increased in severity)	28	93.3
Decreased need for sleep	27	90.0
More talkative and/or pressured speech	24	80.0
Inflated self-esteem or grandiosity	22	73.3
Irritability	22	73.3
Verbal/physical aggression (newly emerged or increased in severity)	21	70.0
Excessive money consumption	17	56.7
Flight of ideas, racing thoughts	15	50.0
High risk activities (spending the night outside, running away from home, reckless driving, involvement in risky/ unapproved peer environment)	15	50.0
Expansive/dysphoric mood	14	46.7
Expansive/euphoric mood	13	43.3
Distractibility	13	43.3
Depressive symptoms (crying, unhappiness, worthlessness, guiltiness, thought of death, suicidal ideation, suicide attempt)	12	40.0
Hypersexuality/inappropriate sexual behaviors	9	30.0
Increased religiosity	9	30.0
Changes in appearance (i.e. excessive make up, bizarre clothing)	8	26.7
Use of cigarette, alcohol or substances for the first time	8	26.7
Increase in goal-directed activities or special interests	7	23.3

and combined sessions. This study was approved by Istanbul Medical Faculty's Ethics Committee.

Statistical Analysis

MedCalc statistical software (v12.3.0) was used for statistical analysis. We used means and percentages for descriptive statistics. Because of the limited number of the subjects we did not perform any comparison between different subgroups (i.e. male vs female, or bipolar subtypes).

RESULTS

Socio-demographics of the subjects

Thirty subjects, 19 males (63.3%) and 11 females (36.7%) with an age range of 11 to 18 years (14.87±1.94 years), were included in the study. Seventeen subjects (56.7%) had a normal IQ, 8 subjects (26.7%) had a borderline IQ, and 5 subjects (16.7%) had mild mental retardation (Table 1).

Phenomenology of bipolar disorder

Twenty-two subjects (73.3%) diagnosed with BD type I, three subjects (10.0%) diagnosed with BD type II, and five subjects (16.7%) diagnosed with BD-NOS were included in the study. Eight subjects (26.7%) were diagnosed with rapid cycling BD (Table 1).

Among those diagnosed with BD type I or II (n=25; 83.3%), the first mood episode was a depressive episode in 12 subjects (48.0%), mixed episode in 8 subjects (32.0%), manic episode in 3 subjects (12.0%) and hypomanic episode in 2 subjects (8.0%). Age range for the first mood episode (depressive, mixed, manic, or hypomanic) among these subjects was 11 to 16 years (12.8±2.25 years), and duration of the first mood episode ranged between 5 and 900 days (125.6±220.5 days). The first mood episode that led to diagnosis with BD type I or II (n=25) (manic, mixed, or hypomanic episode) was a mixed episode in 12 subjects (48.0%), manic episode in 10 subjects (40.0%), and hypomanic episode in 3 subjects (12.0%). Age range for the first bipolar mood episode was 11 to 16 years (13.24±2.35 years), and duration of episode ranged between 3 and 900 days (121.04± 215.83 days) (Table 1).

The number of overall mood episodes was 3 or less episodes in fourteen subjects (46.7%), between 4 and 10 episodes in six subjects (20.0%) and more than 10 episodes in ten subjects (33.3%). Regarding psychotic symptoms during mood episodes, 16 subjects (53.3%) reported perceptual and/or thought disturbances. Eleven subjects (36.7%) had both perceptual and thought disturbance, 3 subjects (10.0%) had only perceptual disturbance and 2 subjects (6.7%) had only thought disturbance. Fourteen subjects (46.7%) did not report psychotic symptoms. The most frequent psychotic symptom was auditory hallucinations (n=13). During the onset or course of the illness 4 subjects (13.3%)

attempted suicide once and 5 subjects (16.7%) twice. Twenty-one subjects (70.0%) had no history of suicide attempt (Table 1). Most frequent symptoms during bipolar mood episodes (mixed, manic, or hypomanic) are shown in Table 2.

Psychiatric comorbidity

Except one subject who received only one comorbid diagnosis, all subjects received multiple comorbid psychiatric diagnosis other than BD (Table 3). We did not include subthreshold diagnoses in the analysis. Frequency of DSM-IV comorbid diagnoses among sample were as follows: major depressive disorder-single episode (n=5; 16.7%), major depressive disorder-multiple episodes (n=11; 36.7%), dysthymic disorder (n=1; 3.3%), panic disorder (n=5; 16.7%), separation anxiety disorder (n=17; 56.7%), social anxiety disorder (n=15; 50.0%), agoraphobia (n=7; 23.3%), special phobia (n=18; 60.0%), generalized anxiety disorder (n=10; 33.3%), obsessive-compulsive disorder (n=13; 43.3%), enuresis (n=5; 16.7%), encopresis (n=1; 3.3%), anorexia nervosa (n=1; 3.3%), attention deficit hyperactivity disorder-combined type (n=15; 50.0%), attention deficit hyperactivity disorder-inattentive type (n=8; 26.7%), oppositional defiant disorder (n=8; 26.7%), conduct disorder (n=2; 6.7%), Tourette disorder (n=5; 16.7%), chronic motor tics (n=5; 16.7%), transient motor tics (n=4; 13.3%), transient vocal tics (n=3; 10.0%), nicotine abuse (n=2; 6.7%), nicotine addiction (n=4; 13.3%), alcohol abuse (n=2; 6.7%), posttraumatic stress disorder (n=2; 6.7%), and autism spectrum disorder (n=2; 6.7%) (Table 3).

The frequency of diagnostic categories from which criteria for at least one disorder met was as follows: depressive disorders (n=16; 53.3%), anxiety disorders (n=28; 93.3%), elimination disorders (n=6; 20.0%), eating disorders (n=1; 3.3%), disruptive behavior disorders (n=23; 76.7%), tic disorders (n=15; 50.0%), substance use disorders (n=7; 23.3%), and autism spectrum disorders (n=2; 6.7%) (Table 3).

Table 3. Comorbid psychiatric disorders

DSM-IV Comorbid diagnoses	N	%
Depressive disorders	*16*	*53.3*
Major depressive disorder-single episode	5	16.7
Major depressive disorder-multiple episodes	11	36.7
Dysthymic disorder	1	3.3
Anxiety disorders	*28*	*93.3*
Panic disorder	5	16.7
Separation anxiety disorder	17	56.7
Social anxiety disorder	15	50.0
Agoraphobia	7	23.3
Special phobia	18	60.0
Generalized anxiety disorder	10	33.3
Obsessive-compulsive disorder	13	43.3
Elimination disorders	*6*	*20.0*
Enuresis	5	16.7
Encopresis	1	3.3
Eating disorders	*1*	*3.3*
Anorexia nervosa	1	3.3
Disruptive behavior disorders	*23*	*76.7*
Attention deficit hyperactivity disorder		
Combined type	15	50.0
Inattentive type	8	26.7
Oppositional-defiant disorder	8	26.7
Conduct disorder	2	6.7
Tic disorders	*15*	*50.0*
Tourette disorder	5	16.7
Chronic motor tic disorder	5	16.7
Transient motor tic disorder	4	13.3
Transient vocal tic disorder	3	10.0
Substance use disorders	*7*	*23.3*
Nicotine abuse	2	6.7
Nicotine addiction	4	13.3
Alcohol abuse	2	6.7
Posttraumatic stress disorder	*2*	*6.7*
Autism spectrum disorders	*2*	*6.7*
Atypical autism	1	3.3
Asperger's syndrome	1	3.3

DISCUSSION

Phenomenology of bipolar disorder in young subjects

BD is a relatively frequent psychiatric disorder with significant impairment in young and very young populations (1–4,28,29). It has been reported and documented that phenomenology of BD may show important developmental differences among young subjects compared to adult patients(3,4,8–15). In this study we investigated many different phenomenological characteristics of pediatric BD such as age at onset, type, duration, symptoms, and number of mood episodes, suicide attempts, prevalence and patterns of psychotic symptoms, and cigarette/alcohol/substance use for the first time during mood episodes. Regarding the age at onset, type, duration, symptoms, and number of mood episodes, findings of the current study have shown generally similar but some different results compared to literature. We would like to discuss several impor-

tant findings of the current study and their clinical implications in the light of relevant literature and clinical practice.

In a recent meta-analysis of the phenomenology and clinical characteristics of mania in young subjects, Kowatch et al. (2005) have reported most frequent symptoms as, in decreasing order, increased energy, distractibility, pressured speech, irritability, grandiosity, racing thoughts, decreased need for sleep and elevated/euphoric mood, poor judgment, flight of ideas and hypersexuality (14). Compared to the study by Kowatch et al., we have reported much more symptoms with detailed description and frequency that were reported or observed during bipolar mood episodes. Majority of the symptoms reported in the current study are consistent with the study by Kowatch et al. and other studies on the phenomenology of BD in young subjects (15,30). An important difference may be the fact that while we have reported a high rate of verbal/physical aggression (70%) during bipolar mood episodes, Kowatch et al. did not include this symptom in their study (14). Verbal and/or physical aggression in these subjects were either emerged or worsened during mood episodes. However aggression, despite not a typical manic symptom, has been reported as high as 90% in young subjects with BD in the literature (3,4,9,15,30).

More than half of the young and adult subjects who were diagnosed with BD were reported to have previous depressive episodes (6–8), and we found that depressive episodes had been the most common mood episodes (40%) before having been diagnosed with BD among subjects in this study. It is clinically well known that depression may precede BD in young subjects (3–8), therefore young subjects with depression should be assessed for the risk of (hypo)mania before starting medical treatment for depression (3,4). Although not typical manic symptoms, psychotic symptoms have been reported in 16 to 60% of young subjects with BD during mood episodes, and auditory hallucinations were the most common psychotic symptoms (3,4,8). A meta-analysis on the phenomenology of pediatric BD has reported 42% of psychotic symptoms (14). Furthermore, a recent study has reported that psychotic symptoms were more frequent in early onset (before 18 years) BD than late onset (above 40 years) BD (47% and 26%, respectively) (13). In the current study we have found a rate of 53% for perceptual and/or thought disturbances and the most common psychotic symptom was auditory hallucinations (43%). Together with some other symptoms (such as irritability, dysphoric mood, abnormalities in behavior and speech) psychotic symptoms may cause a misdiagnosis of psychotic disorder in these subjects (3,4,10,24). Therefore it is important to carefully assess the psychotic symptoms in young subjects with BD both for differential diagnosis and accurate treatment (3,4,10). Young subjects with BD have been reported to have significant rates of suicidal ideation and/or attempts (15,31–33). While suicidal ideation has been reported as high as 94% (31), suicide attempt has been reported in one third of the patients (15,32). Psychotic symptoms and mixed states have been considered particular risk factors for suicidal ideation and/or attempts (31–33). In the current study it is found that during the onset or course of the illness 30% of the subjects had suicide attempts (4 subjects had one attempt and 5 subjects had two attempts). Consistently with the literature, seven out of nine subjects were observed to have psychotic symptoms. Suicide in the young population has been among the major causes of death in many countries (34). Psychiatric disorders, particularly mood disorders, are among the most important risk factors for youth suicide (34). Therefore young subjects with BD, particularly those with psychotic symptoms and mixed states, should be assessed for suicidal ideation and/or plan in terms of suicide prevention (3,4,31–33).

Psychiatric comorbidity in young subjects with bipolar disorder

Psychiatric comorbidity in pediatric BD has been considered to have important research and clinical implications as the etiology and pathophysiology, differential diagnosis, clinical presentation, treatment planning, response to treatment, and long term outcome of the illness may change significantly (3,4,16–25,35). Because studies have consistently shown high rates of psychiatric comorbidity in pediatric BD (3,4,16–25,35), it is suggested that all young subjects diagnosed with BD should be thoroughly assessed for comorbid psychiatric disorders (3,4,10,24,35). However rates and patterns of comorbid psychiatric diagnoses may change across studies mainly depending on the sample

characteristics, referral center, and study methodology (16–25,35).

A very recent review by Frias et al. on the prevalence and impact of comorbid disorders in PBD reported rates of anxiety disorders as high as 41% to 80% (weighted mean prevalence 54%), rates of ADHD of 4% to 94% (weighted mean prevalence 48%), rates of disruptive behavior disorders of 7% to 75% (weighted mean prevalence 31%), rates of SUD of 16% to 48% (weighted mean prevalence 31%) and rates of pervasive developmental disorders (PDD) of 11% to 30% (weighted mean prevalence 19%) (35). They also have reported that evidence indicates that ADHD and anxiety disorders negatively affect the symptomatology, neurocognitive profile, clinical course and the global functioning of PBD (35). Generalized and separation anxiety disorders have been the most frequently reported comorbid anxiety disorders (18,19,35). Few studies that investigated OCD comorbidity in PBD reported rates of 17% to 49% (16,18,30,36). It has been reported that multiple anxiety disorders (≥3), especially generalized anxiety disorder and social phobia, were present at a higher frequency when OCD and BPD were comorbid (37). Sala et al. reported that anxiety disorders usually predate the onset of PBD and are associated with longer duration of mood symptoms, more severe depressions, and family history of depression (19). Furthermore, it has been reported that adolescent anxiety disorders were uniquely associated with increased risk for early adulthood bipolar disorder after adolescent bipolar disorder was accounted for (38). To avoid (hypo)manic switches, psychotherapeutic interventions have been suggested as an alternative treatment for comorbid anxiety and OCD in young subjects with BD (18). Regarding the current study, we have reported high rates of comorbid anxiety disorders (93%) including OCD. Majority of the subjects had multiple comorbid anxiety disorders and the mean number of anxiety disorders was 2.8. Rates and patterns of anxiety disorders and OCD in this sample are generally consistent with the literature. However, despite anxiety disorders have more frequently been reported to be associated with BD type II (15,19), we could not perform such a comparison due to small sample size in BD subtypes. Given the previous literature data, high rates of anxiety and depressive disorders in this sample may be somewhat interrelated.

Comorbidity with ADHD and disruptive behavior disorders (ODD and CD) is a well-known issue in PBD. There have been a number studies on the comorbidity with ADHD and disruptive behavior disorders (DBD) and their impact on the phenomenology, differential diagnosis, treatment, and course of the illness in PBD (3,4,10,13–17,24,30,35,36,39). Of particular interest, ADHD has been reported to be present as frequently as 94% in PBD, and several potential explanations were suggested for this high rate of co-occurrence, such as (1) that BD symptom expression leads to overdiagnosis of ADHD in BPD youth, (2) that ADHD is a prodromal or early manifestation of PBD, (3) that ADHD and associated factors (e.g., psychostimulants) lead to the onset of PBD, and (4) that ADHD and BD share an underlying biological etiology (i.e., a common familial or genetic risk or underlying neurophysiology) (39). Bipolar disorder with comorbid ADHD is considered to be a developmentally specific phenotype of early-onset BD (39). Despite the fact that ADHD, DBD and PBD may have many similar symptoms (such as hyperactivity, impulsivity, excessive and/or pressured speech, irritability, aggression, distractibility) that may lead to mutual misdiagnosis, several important clinical and phenomenological characteristics have been defined as helpful in differentiating ADHD and BD in young subjects (10,24,39). Age at onset and course of symptoms (i.e. episodic vs chronic course), presence of core manic symptoms (such as elevated mood, grandiosity, hypersexuality), and positive family history for BD have been considered in favor of diagnosing BD (10,24,39). Rates of comorbidity for ADHD in PBD have been changed significantly, being reported to change between 4% and 94% (weighted mean prevalence 48%). It is possible that phenomenological and clinical similarities between ADHD and PBD may contributed to these differences across studies. In this study we reported a rate of comorbidity of 76% for ADHD and 26% for DBD, which is very similar to the literature. It may be important to note that ADHD comorbidity may manifest as any subtype in PBD; one third of the subjects diagnosed with ADHD in this study were diagnosed with inattentive type of ADHD.

BD has been reported to be an important risk factor for SUD in young and adult subjects (22,35,40,41).

Rates of comorbidity with SUD have been reported to be as high as 50% in PBD and older age at onset has been an important predictor for SUD (35,40,41). Wilens et al. reported that adolescent BD is a significant risk factor for substance use disorders and cigarette smoking, independently of psychiatric comorbidity (40). Regarding global functioning, most studies have shown greater impairment among bipolar youth with (vs. without) comorbid SUD, mainly legal and academic difficulties (22,35). In the current study we have reported a rate of 23% for SUD comorbidity. Moreover 8 subjects (26%) reported cigarette, alcohol or substance use for the first time during their mood episodes. While some of these subjects discontinued their use of these, the majority continued. Given this observation it may be important to note mood disorders are important risk factors for both starting and continuing SUD among young subjects. It is important to mutually assess SUD in young subjects with BD, and mood symptoms or episodes in young subjects with SUD. Because SUD may complicate clinical picture, treatment compliance, and worsening of mood symptoms, young subjects with BD should receive appropriate psychopharmacological and/or psychosocial interventions if they have comorbid SUD (3,4,35,40,41).

Another important comorbidity in PBD may be autism spectrum disorders (ASD). High rates of aggressive behaviors and severe mood disturbances are documented in children and adolescents with ASD; and a subgroup of these subjects may present with episodic worsening of their symptoms that is clinically consistent with bipolar disorder (41–44). Meanwhile a bidirectional overlap between PBD and ASD was reported as BD occurred in 21% of ASD and ASD occurred in 11% of PBD subjects. In the current study we have reported a rate of 6% for ASD comorbidity and reported the detailed clinical picture of one subject with a comorbid diagnosis of Asperger syndrome elsewhere (44).

CONCLUSIONS AND LIMITATIONS

In this descriptive study we attempted to define several clinical characteristics and psychiatric comorbidity in clinically followed young subjects diagnosed with BD. Previous depressive episodes, mixed mood episodes, and psychotic symptoms were frequently reported characteristics in PBD. Despite BD may frequently manifest in broad phenotype among young subjects, majority of the subjects in this study had DSM-IV-defined BD type I or II. However it may be important to note that many studies on pediatric BD that were cited in this paper have also included subjects with a diagnosis of BD-NOS (15,19,30). This study may have several limitations. Because of the limited number of subjects we could not conduct any analysis between subgroups (i.e. male vs female, bipolar disorder subtypes, or IQ scores). Furthermore information on several illness characteristics (such as age at onset, duration, symptoms, and number of past mood episodes) were coded depending on patients' and families' reports that may have memory biases. We have conducted psychiatric assessment by using a well-known, universally adapted instrument, K-SADS-PL. We have found high rates of psychiatric comorbidity among young subjects with BD. Young subjects diagnosed with BD should also be assessed for comorbid anxiety, OCD, ADHD, and SUD as there may be important research and clinical implications.

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