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Bipolar disorder in children, adolescents, and young adults. Part 1. Clinical symptoms and differential diagnosis. Recommendations under the patronage of the Executive Board of the Polish Psychiatric Association, National Consultants in the field of Psychiatry and National Consultants in Child and Adolescent Psychiatry

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Summary

Bipolar disorder (BD) occurring in children and adolescents may have a different clinical course than that diagnosed in adults, while there are no different criteria in the diagnostic classifications used. Among patients under 18 years of age, irritability, atypical course of depressive episodes, mixed episodes or very rapid phase change are much more frequently observed. Diagnostic difficulties are also overlapped by those resulting from the need to differentiate BD from other disorders which have their onset in childhood and adolescence; the probability of their coexistence should be considered concomitantly. This applies primarily to hyperkinetic disorders, behavioral disorders, borderline personality disorder or addiction to psychoactive substances. About 50% of patients present with symptoms of BD before the age of 18, and it takes on average 5 to 10 years from symptom onset to receive a correct diagnosis. Undiagnosed BD can have a negative impact on the development of emotional, social and cognitive competences, significantly affecting a patient's functioning into adulthood. That is

why it is so important for specialists working with children and adolescents to be aware of the differences in the clinical course of BD and to make the right diagnosis, taking into account the biological, developmental and systemic context.

Key words: bipolar disorder, affective symptoms, children, adolescents

Introduction

For many years, bipolar disorder (BD) was thought to occur rarely in children and adolescents. However, following the Second World War, in subsequent generations, an increase in the incidence of bipolar disorder among people under 18 years of age began to be observed, as well as an increase in the diagnosis of its first episode at increasingly younger ages [1]. Despite differences in the clinical picture of BD in the classifications of mental disorders and diseases, there are still no separate diagnostic criteria for the pediatric population. The clinician–diagnostician must demonstrate knowledge of the physiological development of children and adolescents in order to match the criteria to both chronological and developmental age.

1. Prevalence of bipolar disorder among children and adolescents

Available research findings indicate that the prevalence of BD among children and adolescents varies from country to country [2]. Depending on the method used and the diagnostic criteria, it is estimated to range from 1% to 15% [3-5]. Studies assessing the prevalence of BD among children and adolescents estimated that it occurs in 0.1% of the population aged 9 to 13 years; 1.2% of individuals aged 8 to 19 years; and 2.9%–6.7% in patients aged 14 to 18 years [6, 7]. Based on a meta-analysis conducted by Van Meter et al. [8], the average prevalence rate of the spectrum of affective disorders in the pediatric population was 1.8%, and for type I BD, it was 1.2%, with a higher prevalence observed in older age groups. In Poland, based on the results of the EZOP II studies [9] conducted from 2017 to 2019, the onset of a manic episode was confirmed in 1.6% of children aged 7 to 11 years, slightly more often in girls than in boys. In 3.7% of adolescents (aged 12 to 17 years), manic episodes have occurred at some point in their lifetime. This estimate indicates a higher prevalence of mood disorders in boys than in girls: 3.7% vs. 2.8%; however, these differences did not reach the level of statistical significance. Based on data published by the Central Office of the National Health Fund over the last six years, there has been a significant increase in the number of children and adolescents diagnosed with F30-F31 using publicly funded healthcare services – from 843 in 2014 to 2,418 in 2022 [10].

Retrospective studies in the USA show that about 60% of adults diagnosed with BD had symptom onset before the age of 20, and up to 20% had onset before the age of 10 [11, 12]. A questionnaire conducted in 12 European countries showed that 33.1% of adult patients with BD (aged 18-83 years) reported onset of the illness before the age of 20 [11]. It is reported that the peak incidence of BD falls between the ages of

15 and 25 years [12]. Onset before the age of 19 was found in 50%–66% of cases [13], and before the age of 13 – in 18% [14]. According to one approach in American psychiatry, BD can be diagnosed in children under 10 years of age [12, 15], whereas in Europe, this still remains a matter of debate [16, 17]. Available findings from studies comparing patients from the USA and Europe indicate that early-onset BD accounts for 63%–68% of cases in the USA, compared to 25%–42% in Europe. Onset before the age of 13 was found in 31.1% of cases in the USA, and 5.6% in Europe. Between the ages of 13 and 18, onset was reported in 38.1% of cases in the USA, and 26.6% in Europe. In the USA, more than two-thirds of the study participants were diagnosed with onset of the disorder in childhood or adolescence, compared to only one-third in Europe [18].

2. Diagnostic difficulties and clinical symptoms of bipolar disorder in children and adolescents

The diagnostic criteria for BD in the DSM-5 and ICD-11 classifications are, for the pediatric population, largely the same as for adults. In DSM-5, for a depressive episode in children and adolescents, two clinical differences are specified – depressed mood may be replaced by irritable mood, and weight loss is replaced by the criterion of a lack of expected weight gain. However, the results of many studies conducted to date indicate much greater differences in the course of BD in children and adolescents compared to adults.

One of the predominant symptoms of mania in BD in the pediatric population is irritability [19]. Woźniak et al. [20] showed that in cases of abnormal mood in children and adolescents, irritability was observed in 94% of patients and was significantly more frequent than euphoria (51%). Irritability may also be present during depressive or mixed episodes. Aggressive and self-aggressive behavior may coexist with it. It can also occur as a normative feature at many stages of development in children and adolescents. In addition, it may appear in the course of other mental disorders characteristic of this developmental period. However, irritability that occurs in a cyclic pattern along with other symptoms of mood disorders should always be the basis for a thorough assessment for BD, with particular attention to the family history of mental disorders.

In numerous studies it has been proven that, apart from irritability, the most common symptoms of mania among children and adolescents include excessive energy, increased activity, flight of ideas, racing thoughts, and grandiosity [8, 21, 22]. Grandiose delusions or other psychotic symptoms are less common. It is worth noting that grandiosity can also present diagnostic difficulties and is often not recognized as a symptom of BD. Children may fantasize about being exceptional or highly accomplished, while adolescents may display narcissistic attitudes and behaviors, which can still fall within the range of normative development. However, high variability in self-perception accompanied by other symptoms of mood disorders should also be a signal to broaden the diagnostic assessment for BD.

Sleep disturbances are symptoms that may facilitate the diagnosis of a manic episode in BD. They may be considered a variant of the broad developmental norm in adolescents or may occur in the course of other mental disorders. However, in these situations, they are usually associated with a feeling of fatigue rather than with restfulness or excess energy. When a manic episode is suspected, it is also worth paying attention to hypersexuality, especially when it appears in the absence of any indications of suspected sexual abuse or exposure to pornography.

As is known, in patients under 18 years of age, BD usually begins with an episode of depression. Studies show that episodes of depression among children and adolescents are more often atypical, accompanied by hypersomnia and hyperphagia, and follow a more severe course than those occurring in the adult population [23]. Moreover, it has been shown that in up to 70% of affected adolescents, mood may change every few days – or even multiple times a day – and they may experience several episodes of mood disorders within a year [24]. Therefore, in the course of BD, mixed states are diagnosed significantly more often in children and adolescents. In addition, a very rapid phase shift is observed – one not described in any diagnostic classification – and is often categorized as other or unspecified affective disorders.

This atypical yet common presentation of BD in children and adolescents is associated with developmental differences of the central nervous system, which influence symptom expression and the observed evolution of the disorder's clinical picture. Table 1 summarizes the symptoms of BD during development.

Table 1. **Symptoms of BD during the development period**

BD	Depression/mixed states	Mania/hypomania	Euthymia
Irritability	+	+ 94% [20]	+ 51% [20]
Excessive energy		+ [8, 21, 22]	
Flight of ideas, racing thoughts		+ [8, 21, 22]	
Increased activity		+ [8, 21, 22]	
Grandiosity		+ [8, 21, 22]	+ (as hypomanic defence)
Narcissistic behavior			+ (as hypomanic defence)
Sleep disturbances	Excessive daytime sleepiness, early morning awakening	Sleep disturbances combined with restfulness or excess energy	Sleep disturbances – prolonged second phase of falling asleep
Hypersexuality		+	
Hyperphagia	+		+ (as emotional defense)

3. Comorbidity and differential diagnosis of bipolar disorder in children and adolescents

The diagnostic difficulties described above in children and adolescents are additionally overlapped by those arising from the need to differentiate BD from other, often co-occurring, disorders. These include hyperkinetic disorders (ADHD), behavioral and oppositional defiant disorders, borderline personality disorder, and psychoactive substance abuse. In addition, BD often coexists with anxiety disorders, eating disorders, autism spectrum disorders, and others. Comorbidity and differential diagnosis are shown in Tables 2 and 3.

One of the most common co-occurring diagnoses with BD is ADHD. Patients diagnosed with both conditions often experience rapid mood swings and high impulsivity, along with behavioral variability. Coexisting behavioral disorders can further hinder proper diagnosis. Overlapping symptoms of behavioral disorders, including oppositional defiant disorder and BD, include irritability, hostility, and impulsivity. Sexual disinhibition and behaviors resulting from impulsivity are very often interpreted as acts of breaking social norms within the context of behavioral disorders, rather than as symptoms of BD, which can lead to a misdiagnosis. Tantrums or aggressive behavior may overlap with symptoms of mixed or manic states.

In both adults [25] and adolescents [26], the co-occurrence of BD and borderline personality disorder is associated with a more severe course and worse prognosis. It is worth noting that affective disorders are linked to an increased risk of borderline personality disorder. Moreover, BD is more likely to develop in individuals with borderline personality disorder than with other personality types [27]. The first symptoms of personality disorders usually appear during adolescence. Mood instability and variability in functioning are also features of affective disorders. When cyclothymia is also considered in the differential diagnosis – an affective disorder that is extremely rarely diagnosed – the correct diagnosis becomes even more complicated. Researchers [28] point out that cyclothymia is characterized by a chronic course, with typical symptom variability, the severity of which does not meet the criteria for other affective disorders, and for which remission is difficult to achieve. Due to the overlap of symptoms of BD, personality disorders, and cyclothymia, it may happen that in the early stages of the disorder, before the emergence of the full clinical picture, diagnostic resolution is impossible.

Many months of abuse of various psychoactive substances can mask the symptoms of BD, making it difficult to determine whether the presented symptoms are a complication of substance use or whether the psychoactive substance was used as a way to alleviate mood swings. This usually requires a detailed interview with both the patient and people from the patient's environment, as the clinician must keep in mind that the coexistence of these two disorders has significant therapeutic implications.

Among other disorders co-occurring with BD, anxiety disorders should also be mentioned, the most common of which are generalized anxiety disorder, separation anxiety disorder, panic disorder, and social phobia. The former two are more common

among children, while the latter two are more common among adolescents; overall, anxiety disorders are more prevalent in girls [29]. Some researchers [30] suggest that anxiety symptoms may represent the clinical picture of the prodromal phase of BD – in retrospective studies, up to three-quarters of patients reported experiencing anxiety before developing the disorder. However, it should be noted that anxiety is a non-specific symptom that may also precede the onset of other mental disorders [31].

Table 2. **Comorbidity and differential diagnosis**

BD	Comorbidity	Differential diagnosis
ADHD	+ 50% of patients [32]	+
Behavioral disorders, including oppositional defiant disorder	+ 30% of patients [32]	+
Borderline personality disorder	+ 20% of patients [33]	+
Harmful use or abuse of psychoactive substances	+ 30% of patients [34]	+
Anxiety disorder	+ [35-37]	
Eating disorder	+	
Autism spectrum disorder	+	

Table 3. **Differentiating symptoms of BD and ADHD, behavioral disorders including oppositional defiant disorder, and borderline personality disorder**

BD	Overlapping vs. differentiating clinical symptoms
ADHD	**Overlapping symptoms:** psychomotor hyperactivity, impulsivity, tendency to engage in risky behaviors, distractibility, rapid speech **Differentiating symptoms:** increase in goal-oriented activity, grandiose attitude, racing thoughts, decreased need for sleep, sexual behaviors
Behavioral disorders including oppositional defiant disorder	**Differentiating symptoms:** behavioral disorders are usually a continuous and progressive process, whereas clinical symptoms in BD appear cyclically and vary over time
Borderline personality disorder	**Overlapping symptoms:** emotional lability, impulsivity, autoaggressive behavior, increased risk of psychoactive substance use, mood swings **Differentiating symptoms: a** specific way of experiencing oneself and the world, intense but unstable interpersonal relationships, chronic course with fear of rejection and feelings of emptiness, lack of episodicity in sleep, mood, and appetite

4. Suicide and affective disorders in children and adolescents

In 2006, Bridge et al. [38] published a comprehensive review of epidemiological and research data on the risk of suicide in adolescents. According to the researchers, nearly 90% of the victims suffered from mental disorders. Among the disorders associated with a clearly increased risk of suicide, BD was, of course, mentioned. Miranda-Mendizabal et al. (2019) [39] conducted a meta-analysis of studies on this phenomenon among adolescents. It was confirmed that the risk of suicide attempts is higher in women and girls, while the risk of completed suicide is higher in the male gender. In this work, the risk of suicide attempts was associated (among other factors) with affective disorder in girls. Completed suicide was associated with any mental disorder in both sexes. BD was not mentioned here as a specific risk factor.

A meta-analysis of the occurrence of suicidal thoughts and suicide attempts in adolescents with mood disorders was also presented by De Crescenzo et al. (2017) [40]. For bipolar depression, the risk was 31.5%, for unipolar depression 20.5%, and for mania or hypomania without depression – 8.5%. Different results were obtained by Patel et al. (2020) [25], who analyzed records of more than 130,000 adolescents hospitalized with a diagnosis of either unipolar or bipolar depression. According to these authors, the incidence of suicidal thoughts, behaviors, and suicide attempts was higher in unipolar depression. More recent data were presented by Serra et al. (2022) [41]. A systematic review of 41 studies involving 104,000 adolescents indicated that 26.2% of patients with depression in the course of BD and 12.5% of those with unipolar depression had made suicide attempts (at least once in their lifetime). However, the prevalence of suicide attempts during the follow-up period was similar in both groups. These data represent a summary of all the studies analyzed. In studies directly comparing patients with unipolar and bipolar depression, the risk of suicide attempts was higher among those diagnosed with BD. The researchers also analyzed the ratio of suicide attempts to completed suicides, which was 50 and significantly lower than the estimate for the general population (about 250). However, in adults with the disorder, this ratio is even lower (indicating greater lethality of suicide attempts), ranging from 5 to 20.

In 2012, a review of literature prepared by Halfon et al. [42] was published. The researchers analyzed factors related to the severity of suicidal tendencies in BD. Among the factors associated with a higher risk of suicide attempt were the onset of the illness before the age of 12 and the period of adolescence; data on gender were inconclusive. The clinical factors included BD type I, a mixed state, the severity of the depressive episode, the presence of psychotic symptoms, as well as the co-occurrence of other mental disorders and a cyclothymic temperament. A risk factor for suicide attempts was previous suicidal thoughts and behaviors.

It is worth noting that the literature data refer primarily to suicide attempts and suicidal tendencies. Data on factors related to completed suicide are scarce.

To reduce the risk of suicide, researchers recommend screening, early detection of the illness, and treatment. Among medicinal products, lithium is mentioned as a drug

with specific anti-suicidal effect. However, data on the effectiveness of these strategies in the pediatric population are limited.

5. Diagnostic variability of bipolar disorder across the lifespan

Bipolar disorder is characterized by high recurrence, early onset, familial occurrence and a tendency to progression. The average time between the onset of the illness and a proper diagnosis is estimated at 5 to 10 years [43]. Within the first year of psychiatric treatment, only 20% of patients experiencing a depressive episode in the course of BD receive an accurate diagnosis of bipolar disorder [43, 44]. More than 60% of individuals later diagnosed with BD report having previously received between one and four other diagnoses [45], and up to one-third of patients may be misdiagnosed for 10 years or longer [46]. Based on a project conducted in 2000 by the National Depressive and Manic-Depressive Association (NMDA), it was found that BD was most frequently confused with unipolar affective disorder/recurrent depressive disorder (60%) [44]. It is estimated that up to 20%–30% of patients presenting to primary care physicians with depressive or anxiety symptoms may in fact suffer from BD [47, 48].

In particular, early-onset BD is associated with a number of challenges associated with early diagnosis and treatment. In children from so-called high-risk groups, associated with a positive family history of the illness (i.e., a diagnosis of BD in one parent), symptom evolution may occur – from the initial onset of anxiety disorders, through depression, and eventually to bipolar disorder [49]. In American cohorts, this has been associated with a high risk of developing many early prodromal symptoms, including anxiety, ADHD, oppositional defiant disorder, and depression, followed later by BD [50].

A change in the diagnostic criteria for BD in the new ICD-11 classification, compared to the previously used ICD-10, may affect the frequency of this diagnosis. Although BD is often an "underdiagnosed" disorder (especially in the population of patients with recurrent depression), reports of its "overdiagnosis" are appearing more frequently in the literature [51], e.g., among patients with personality disorders (in particular borderline personality type) [34], among individuals abusing psychoactive substances [52] or in children with ADHD symptoms [35]. However, the diagnosis of BD does not exclude the possibility of comorbidity with these disorders, as described in the previous section.

Summary

Most studies published over several decades indicate that BD is a fixed diagnosis with a variable clinical picture depending on age. The most important clinical predictors of bipolar disorder spectrum development are anxiety symptoms, early depression, affective lability, periodic attention difficulties, and episodic aggression [45]. Alarming signals in young people include sleep disturbances, changes in energy levels, and im-

paired school and socio-emotional functioning. An increased risk of the illness occurs in young people whose parents suffer from BD. In addition, individuals who respond to antidepressant or psychostimulant treatment with excessively elevated mood and drive require special attention. Patients with onset in childhood or adolescence report more episodes, more comorbidities, and more rapid cycle changes. Prospectively, they also show more severe courses of mania and depression, and shorter periods of remission. They are also at an increased risk of substance abuse and other comorbidities, and at a higher risk of suicide attempts over their lifetime. Therefore, in light of the presented facts based on reliable scientific research, clinicians should be open to considering a diagnosis of BD in each age group, bearing in mind the clinical difference of this disorder in the pediatric population and the complications of misdiagnosis. The diagnosis of BD and its differentiation should be based on clinical symptoms, course, family history, and often also on the responsiveness to the treatment used. Late detection of bipolar disorder symptoms and diagnosis, and consequently – proper treatment, entails significant clinical consequences, i.e., a higher number of relapses, increased frequency of suicide attempts and hospitalizations, development of treatment resistance, and a higher risk of rapid phase changes [46, 48]. Patients respond better to treatment in the early stages of the disease. Early diagnosis and treatment of BD in adolescents is crucial because childhood onset of the illness, compared to adulthood, is associated with a more problematic course, increased substance abuse, suicide risk, and more severe episodes of mood disorders in adulthood [13, 53].

The lack of intensive, comprehensive treatment is associated with an increased risk of not only relapses and social and educational dysfunction, but also cognitive dysfunction if subsequent episodes occur within a year after the first manic episode [54, 55]. Given that the number of previous episodes is associated with the degree of cognitive dysfunction and the development of treatment resistance, prevention of episodes from the very beginning becomes the main goal of treatment [56]. However, clinical trials and systematic reviews on the treatment of children and adolescents are still lacking, and current guidelines are largely based on expert opinions.

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