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ORIGINAL ARTICLE

Early-onset psychosis: What is the diagnostic outcome?

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Abstract
Background and objectives: Schizophrenia and bipolar disorder may show overlapping symptom profiles especially in early-onset cases. The aim of this study was to establish a final diagnosis, examine possible similarities and differences in symptom presentations, and overall functioning of patients with early-onset psychotic episode.
Methods: Adolescents, presenting with at least one psychotic symptom, who were clinically followed up for at least 6 months, constituted our sample. Psychiatric diagnoses were established by using Schedule for Affective Disorders and Schizophrenia for School Aged Children Present-Lifetime Version (K-SADS-PL), psychotic symptoms were assessed by Positive and Negative Syndrome Scale (PANSS), and level of functioning was determined by Children's Global Assessment Scale (CGAS).
Results: Of 51 patients, 55% received a diagnosis of Psychotic Disorder (PD) and 45% a Mood Disorder (MD). Besides a major overlap in symptom presentation, there were significant differences in distribution. Hallucinations, disorganized speech, and withdrawal/isolation were encountered significantly more in the PD group, whereas hyperactivity, increased speech, and aggression were significantly more frequent in the MD group. PANSS positive, negative, and general psychopathology scores were significantly higher in the PD group. The difference was more pronounced in terms of PANSS negative scores. Overall functioning was similar in two groups.
Conclusions: Adolescents with early-onset psychotic episodes present with a combination of psychotic and mood related symptoms. Initial assessments may have the risk of misdiagnosis. During follow-up, clinicians should not underestimate the possibility of a mood disorder with psychotic features, whereas negative psychotic symptoms may have a discriminative value in favor of psychotic disorders.

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Introduction

In current operational classification systems, DSM-V (Diagnostic and Statistical Manual of Mental Disorders-V) and ICD-10 (International Classification of Diseases-10), psychotic illnesses are described as distinct categorical conditions.[1,2] Rooting from ''Kraepelinian dichotomy'', this categorical approach assumes that schizophrenia and affective disorders can be clearly distinguished. On the other hand, in the last two decades the family, twin, and whole-genome linkage studies increasingly have shown that there has been an overlapping genetic background for schizophrenia (SCZ) and bipolar disorder (BD).[3] Due to the underlying polygenic etiology and similar genetic insults, the two disorders are considered to share a common neurodevelopmental etiological model with a typical onset in late adolescence or early adulthood. In addition, studies revealed that many patients with first-episode psychosis, especially the early onset adolescent cases had common clinical features of schizophrenia and bipolar disorder.[4,5] These findings led many clinicians to argue for a dimensional approach for psychotic illnesses where schizophrenia and bipolar disorder are standing at the two ends of the continuum.[6,7] Among these, Bipolar and Schizophrenia Network for Intermediate Phenotypes (BSNIP) consortium refers to the concept of psychosis as a broad clinical phenotype.[8] Also, several symptom dimensions have been proposed to better formulate clinical psychosis phenotype.[9,10] Nevertheless, many other researchers argue in favor of the ''Kraepelian dichotomy'' and find categorical approach more useful.[11]

Around 11–18% of patients with psychosis experience their first-episode of before age 18.[12] These so called ''early-onset psychosis'' cases represent the most heterogeneous group with overlapping symptoms and clinical characteristics.[5,13,14] Psychotic symptoms per se are not pathognomonic of a specific disorder. They may be encountered in other psychiatric disorders, more frequently in affective and anxiety disorders.[15] Thus, many of the adolescents presenting with psychotic symptoms fail to fit into a specific diagnosis at the time of the initial presentation. Uncertainty of the diagnosis during acute episodes necessitates clinical follow-up to ascertain the diagnosis.[16] This variance in clinical presentation and the symptomatic overlap may lead to a low diagnostic stability during the follow-up[17,18] and there is a risk of misclassification at early stages of psychotic disorders.[16] Although there is a growing effort and accumulating knowledge to define the features of psychosis as a broad clinical phenotype, we still need diagnostic categorical criteria for clinical practice. Guidelines underscore importance of adherence to diagnostic criteria and periodic re-evaluations to enhance diagnostic accuracy.[19,20]

The aim of this study was to follow-up a heterogeneous group of patients whose initial presentation was a psychotic episode, and after establishing psychiatric diagnoses, to examine possible similarities and differences in symptom presentations, overall functioning, and other clinical characteristics.

Material and methods

Participants

In this observational study, patients were recruited from Marmara University Child and Adolescent Psychiatry Clinic within a three-year period (2014–2017). All patients, presenting with a psychotic episode (presence of at least one psychotic symptom; hallucinations, delusions, disorganized behavior, disorganized speech or withdrawal/isolation) who were clinically followed up for at least 6 months (up to 72 months) constituted our sample. The age range of the sample was 14–17 years. The exclusion criteria were: presence of mental retardation, pervasive developmental disorders, and significant neurological illness, including history of head injury leading to loss of consciousness.

The study was approved by Marmara University Ethical Committee (09.2017.268). Patients and parents gave written informed consent for the participation in the study.

Measures

Schedule for Affective Disorders and Schizophrenia for School Aged Children Present-Lifetime Version (K-SADS-PL)

The psychiatric diagnoses were established by using Turkish version of K-SADS-PL.[21,22] It is a semi-structured diagnostic interview designed to assess current and past episodes of psychopathology in children and adolescents, according to DSM-IV criteria.

Positive and Negative Syndrome Scale (PANSS)

The psychotic symptoms were assessed by using Turkish version of PANSS.[23,24] This semi-structured interview scale evaluates positive and negative symptoms and general psychopathology. Higher ratings reflect greater severity of symptoms.

The Children's Global Assessment Scale (CGAS)

CGAS is a clinician-rated scale evaluating overall well-being and functioning, where higher scores indicate higher levels of functioning.[25] It has been regarded as a useful measure of overall severity of disturbance in children.

Procedure: The adolescents, presenting with a psychotic episode assessed by clinical psychiatric interview in the first admission. Additional clinical information and history of the symptoms were gathered from the parents. According to the needs of the patients, medical treatment and supportive therapy were initiated. During the follow-up, consensus diagnoses were determined by using K-SADS-PL, which is a semi-structured clinical interview conducted with the adolescents and the parents. The other semi-structured interview scale, PANSS, was used to evaluate the severity and the distribution of psychotic symptoms. PANSS items are scored along a continuum of severity between

1 (asymptomatic) and 7 (extreme symptom severity). General functioning of the patients was assessed by using CGAS, which is a clinician rated scale. According to the score, one of ten categories is established, ranging from 'extremely impaired' (1–10) to 'doing very well' (91–100). To compare symptom presentations, overall functioning, and other clinical characteristics, patients were grouped under two main diagnostic groups; Psychotic Disorder (PD) and Mood Disorder (MD).

Statistical analysis

The data were evaluated using the Statistical Package for the Social Sciences (version 20) program. Descriptive statistics were shown as mean – standard deviation or frequency (%). A 95% confidence interval was used to assess the data. The chi-square test was applied to categorical variables when comparing gender, parental work status, parental education levels, symptom distributions, and classes of pharmacologic treatment between two groups of adolescents. Effect of gender on symptom distributions was evaluated by Binary logistic regression analysis. Student *t*-test was used while evaluating scores of PANSS and CGAS. Means of PANSS and CGAS scores were adjusted for gender by one way analysis of covariance. Pearson correlations were computed between PANSS and CGAS scores. Significance was set at $p < 0.05$ and all p values were two-tailed.

Results

Overall sample was composed of 51 adolescents who had admitted to hospital with a psychotic episode. Of these, 28 patients (55%) constituted Psychotic Disorder group (PD) and 23 patients (45%) constituted Mood Disorder group (MD). The mean age of all patients was 14.76 ± 1.64 years (min 14–max 17 years) and 62.7% ($n = 32$) of all cases were female. The demographic variables of the groups were presented in Table 1. The only significant difference detected between the groups was gender, with the MD group (82.6%) including more females than the PD group (46.4%) ($p < 0.01$). There were no significant differences between two groups in terms of parental education levels and vocational status ($p > 0.05$). In both groups, most of the mothers and fathers were primary school graduates. Most of the fathers were employed whereas most of the mothers were unemployed.

Distribution of psychiatric diagnoses, based on DSM-IV criteria were presented in Table 2. A major overlap in symptom presentations was remarkable, with significant differences in distribution (Table 3). Hallucinations (85.7% vs 47.8%; $p < 0.01$), disorganized speech (53.6% vs 21.7%; $p < 0.01$), and withdrawal/isolation (57.1% vs 21.7%; $p < 0.05$) were encountered significantly more in the PD group, whereas sleep problems (68.2% vs 100%; $p < 0.01$), hyperactivity (11.5% vs 60%; $p < 0.01$), increased speech (4.5% vs 45.5%; $p < 0.05$), and aggression (30.4% vs 66.7%; $p < 0.05$) were significantly more frequent in the MD group. However, the difference for sleep problems was no longer significant when the gender was controlled.

PANSS negative scores ($p < 0.01$) and PANSS general psychopathology scores ($p < 0.001$) showed a moderate to high level of negative correlation with CGAS scores (Table 4).

Table 1 Demographic variables.

	Psychotic disorder	Mood disorder	*p*
Age (M ± SD)	14.82 ± 1.65	14.69 ± 1.66	0.78
Female n (%)	13 (46.4)	19 (82.6)	0.008*
Maternal age (M ± SD)	42.62 ± 5.93	42.25 ± 5.37	0.82
Paternal age (M ± SD)	47.00 ± 5.23	47.26 ± 6.14	0.88
Number of children (M ± SD)	2.88 ± 1.14	3.22 ± 1.54	0.37
		n (%)	
Parental marital status			
Together	22 (84.6)	17 (77.3)	0.71
Maternal education			0.45
Illiterate	1 (4)	3 (14.3)	
Primary school	18 (72)	13 (61.9)	
High school	6 (24)	5 (23.8)	
Maternal vocational status			0.96
Employed	7 (28)	6 (28.6)	
Unemployed	18 (72)	15 (71.4)	
Paternal education			0.95
Illiterate	1 (4)	1 (5)	
Primary school	16 (64)	12 (60)	
High school	8 (32)	7 (35)	
Paternal vocational status			0.27
Employed	21 (80.8)	14 (66.7)	
Unemployed	5 (19.2)	7 (33.3)	

* $p < 0.01$.

Table 2 Distribution of psychiatric diagnoses.

	n (%)
Psychotic disorder	
Schizophreniform disorder	22 (78.6)
SCZ	2 (7.1)
Brief psychotic disorder	2 (7.1)
Substance-related psychosis	2 (7.1)
Mood disorder	
BD-manic episode	9 (39.1)
Depression with psychotic features	6 (26.1)
BD-NOS	5 (21.7)
BD-mixed episode	3 (13.1)

Note: SCZ: Schizophrenia; BD: bipolar disorder; NOS: not otherwise specified.

PANSS and CGAS scores were presented in Fig. 1. PANSS positive ($p < 0.01$), negative ($p < 0.001$), and general psychopathology ($p < 0.05$) scores were significantly higher in the PD group. The difference was still significant even when gender was used as a covariate. Overall functioning as measured by CGAS was similar in two groups. However, number

Table 3 Distribution of symptoms by major diagnostic groups.

	Total *n* (%)	Psychotic disorder *n* (%)	Mood disorder *n* (%)	$\chi 2(p)$ Unadjusted	Odds ratio (95% CI) Adjusted[a]
Psychosis related symptoms					
Hallucinations	35 (68.6)	24 (85.7)	11 (47.8)	6.75 (0.004)**	0.08 (0.01–0.48)**
Disorganized behavior	33 (64.7)	19 (67.9)	14 (60.9)	0.27 (0.60)	0.78 (0.22–2.70)
Delusions	23 (45)	16 (57.1)	7 (30.4)	3.63 (0.056)	0.33 (0.09–1.17)
Disorganized speech	20 (39.2)	15 (53.6)	5 (21.7)	5.36 (0.021) *	0.13 (0.03–0.57)**
Withdrawal/Isolation	21 (41.2)	16 (57.1)	5 (21.7)	6.53 (0.011) *	0.19 (0.05–0.74)*
Mood related symptoms					
Sleep problems	36 (70.5)	15 (68.2)	21 (100)	7.98 (0.009) **	– (0.00–)
Sadness	28 (54.9)	11 (52.4)	17 (77.3)	2.93 (0.087)	1.98 (0.46–8.39)
Hyperactivity	15 (29.4)	3 (11.5)	12 (60)	9.97 (0.001) **	15.86 (2.77–9.79)**
Increased speech	11 (21.5)	1 (4.5)	10 (45.5)	9.81 (0.002) **	16.0 (1.72–149.31)*
Other symptoms					
Aggression	21 (41.2)	7 (30.4)	14 (66.7)	5.77 (0.016) *	4.94 (1.22–19.97)*
Self-mutilation	18 (35.2)	10 (41.7)	8 (36.4)	0.13 (0.71)	0.47 (0.12–1.84)
Suicidal behaviors	10 (19.6)	5 (21.7)	5 (23.8)	0.02 (0.87)	0.56 (0.11–2.71)
Obsessions	9 (17.6)	5 (19.2)	4 (18.2)	0.009 (0.92)	1.87 (0.33–10.47)
Dissociative symptoms	7 (13.7)	5 (19.2)	2 (9.1)	0.98 (0.42)	0.26 (0.04–1.64)

* $p < 0.05$.
** $p < 0.01$. [a]Adjusted for gender.

Table 4 Correlations between PANSS scores and CGAS scores.

		PANSS positive	PANSS negative	PANSS general psychopathology
CGAS	*r*	−0.254	−0.421	−0.551
	p	0.11	0.007*	0.000**

r = correlation coefficient.
* $p < 0.01$.
** $p < 0.001$.

of patients with CGAS score ≤40, designating serious dysfunction, was more in the PD group (7 vs 3).

Clinical characteristics that might be related to the overall functioning such as ''need for hospitalization'' and ''school drop-out'' were assessed. Although the differences were not statistically significant, more patients in the MD group (34.8% vs 21.4%) needed hospitalization and more patients in the PD group (37% vs 13%) dropped out school.

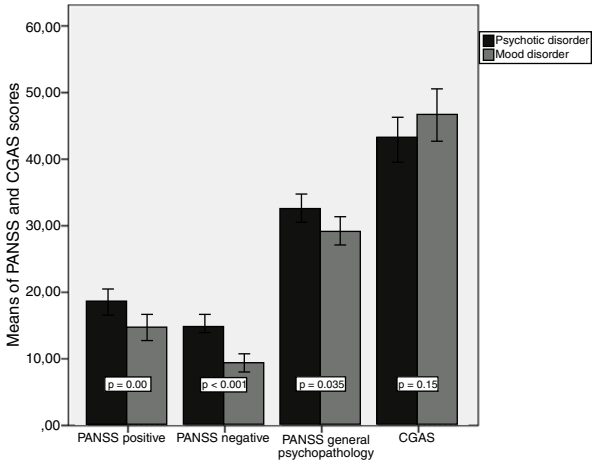

Figure 1 Comparison of PANSS scores and CGAS scores for the groups. Means adjusted for gender.

All the patients were receiving atypical antipsychotic agents (AAP). As a combination treatment, significantly more patients in the MD group were on mood stabilizers (MS) (39.1% vs 17.9%) ($p < 0.01$).

Discussion

Adolescent patients presenting with a psychotic episode who were followed up at least for 6 months were the sample of this study. After DSM-IV diagnoses were established symptom presentations, overall functioning, and other clinical characteristics were assessed.

In our sample, nearly half of the patients with an initial psychotic episode received a diagnosis of a mood disorder. Many studies have shown that patients with first-episode psychosis had common clinical features of SCZ and BD, and the two disorders frequently showed overlapping symptom profiles especially in early onset cases during the adolescence.[4] Depending on the accompanying symptoms, such as psychotic features, correct diagnosis of BD became difficult, often with a delay after the onset of symptoms.[26] In a retrospective chart review, the authors reported that 61.5% of the adult patients with BD had received a first diagnosis different from BD, and the most frequent diagnosis was delusional disorder (17.9%).[27] The rates of psychosis in early onset BD samples was highly variable (24%–62%).[4] For example, in Course and Outcome of Bipolar Youth Study (COBY), psychotic features were present in 34.5% of the subjects with bipolar I disorder.[28] Especially, in bipolar youth with positive family history of psychosis, clinicians were recommended to be alert about the presence of psychotic symptoms.[29] Moreover, a recent study executing factor analysis of manic symptoms among adolescents with BD, disclosed a disorganized/psychotic factor.[30] When we grouped the symptoms under three main headings: psychosis related, mood related, other symptoms, all symptoms emerged in both groups. This considerable symptomatic overlap between affective and non-affective psychosis were consistent with previous studies.[5] However, there were remarkable differences in the distribution of the symptoms in our sample. First, all the ''psychosis related symptoms'' were more frequent in the PD group, with hallucinations, disorganized speech, and withdrawal/isolation reaching statistical significance. A similar finding was reported in a longitudinal prospective study of early onset psychotic disorder. When compared to patients with BD, patients with SCZ and schizoaffective disorder had higher rates of delusions, bizarre behavior, and negative symptoms.[18] Second, all ''mood related symptoms'' were more frequent in the MD group, with hyperactivity and increased speech reaching statistical significance. Such a finding was not surprising, since symptoms like increased goal-directed activity and talkativeness have long been associated with manic/hypomanic episodes and have been included in the diagnostic criteria. More recently, in DSM-5, in addition to abnormal mood, persistently increased goal-directed activity or energy was incorporated into the criterion A of manic episode.[1] Therefore, presence of a substantial severity of these symptoms may have a possible discriminative feature for BD.

When compared with MD group, our patients in the PD group had more severe positive and negative symptoms as measured by higher PANSS scores. Even when the possible effect of gender was controlled with further analyses, the differences in symptom severity remained unchanged. Similarly, in a study comparing adult patients, whose mean duration of illnesses were 4 years for SCZ, 3 years for BD, patients with SCZ had statistically significant higher PANSS positive and PANSS negative scores.[31] In some other studies, researchers analyzed factor domains (namely negative, positive, excitation, depression and cognition) rather than using raw PANSS scores, to identify the organization of symptoms. When PANSS scores of first-episode psychotic patients were assessed by five-factor analysis, there was an overlap of positive symptoms in SCZ and BD, and negative symptoms in SCZ and depression with psychotic features, however the cognitive disorganization factor was significantly greater in SCZ.[32] A similar finding came from a study of adult patients with BD, where all the factors emerged except for cognitive factor.[33] Closely related to the findings of these two studies, although we did not use factor analysis, the difference in two groups was more pronounced in terms of PANSS negative scores. It could be suggestive of a greater overlap in the severity of positive symptoms and a discriminative value for negative symptoms. In addition, the negative symptoms were found to be correlated with decreased level of functioning. In line with our finding, in a 6-month to 10-year follow-up study of psychotic patients, poorer functioning and greater negative and psychotic symptom ratings predicted a shift to SCZ.[16] Similarly, in a 2-year follow-up study of early-onset psychosis, negative symptoms emerged as the only significant predictor of level of functioning.[34]

Among demographic variables, the only significant finding between groups was gender difference. Females outnumbered males in the MD group, whereas males constituted the majority in the PD group. Gender differences in mental disorders have long been investigated. Besides some uncertainties, several studies indicated that the incidence of schizophrenia especially the early onset forms, was higher in men.[35,36] On the other hand, female dominance in the MD group was inconsistent with previous knowledge. Although depression has been encountered almost 2–3 times more common among female adolescents, an equal gender distribution has been accepted for early onset bipolar disorder.[37,38]

A relatively small percent of patients in both groups needed to be hospitalized, it might be due to the finding that the patients in our sample were in the range of moderate functional impairment. Although the differences were not statistically significant, still more patients in the MD group were hospitalized. Many factors, such as aggression, self-injurious behavior, suicidal ideation or attempt, may play role for the decision of hospitalization. In our sample, aggressive behavior, was noted significantly more in the MD group, which might have contributed to relatively increased need for hospitalization. Presence of psychotic symptoms in adolescents with BD might result in unfavorable outcome measures such as increased psychiatric hospitalizations, self-injurious behavior, suicide attempts. In a large, multicenter study authors reported that one third of the

patients with pediatric BD had at least one suicide attempt in their lifetime. They had higher rates of psychiatric hospitalizations, self-injurious behaviors, and psychosis when compared to non-attempters.[39]

The rates of school dropouts might give an idea about overall functioning of the youth. Although not reaching statistical significance, a relatively high percent of patients in the PD group had left school. Two groups did not significantly differ in terms of level of functioning, however 7 out of 28 patients had scores below 41 in PD group, pointing out a serious dysfunction, whereas only 3 patients in MD group showed serious dysfunction. Due to major impairment of functioning in several areas at home, at school or with peers, patients might end up with school dropouts. It was consistent with the findings of other studies, that recommended to use school dropout as a marker of diverse detrimental social problems in first-episode psychosis.[40]

Regarding the limitations of our study, relatively small sample size was the main limitation. The second, although patients were clinically followed up, the change in PANSS and CGAS scores were not included in the study design. Third, we used PANSS raw scores. Forthcoming prospective studies designed with considerable follow-up timelines, including greater sample size, and using five-factor analytic PANSS scores will be more clarifying and more informative about the possible discriminative features of affective and non-affective psychotic disorders. Despite these limitations, we carried out a detailed assessment during the clinical follow-up, including structured diagnostic instruments and standardized scales.

Conclusions

In this study, we examined the diagnostic outcomes, possible similarities and differences in symptom presentations, overall functioning, and associated clinical characteristics of patients with early-onset psychosis. Our data support the notion that adolescents with early-onset psychotic episodes present with a combination of wide range of psychotic and mood related symptoms. Brief, initial psychiatric assessments may have a potential risk for misdiagnoses, therefore clinical follow-ups are recommended. When dealing with patients with early-onset psychotic episodes, clinicians should not underestimate the possibility of a mood disorder with psychotic features. The presence of significant increase in speech and goal-directed activity may account for a distinguishing feature for bipolar disorder, whereas negative psychotic symptoms may have a discriminative value in favor of psychotic disorders.

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Conflict of interest

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