

Clinical Presentations of Early-Onset Schizophrenia: A 10-Year Retrospective Chart Review

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Objective: To collect and describe the clinical presentations of early-onset schizophrenia in a clinical setting. In addition, the authors aimed to compare the clinical presentations of early-onset schizophrenia (EOS) and very early-onset schizophrenia (VEOS).

Materials and Methods: A 10-year retrospective chart review of early-onset schizophrenia participants, both inpatients and outpatients, who received psychiatric treatments at Ramathibodi Hospital, Bangkok, Thailand between January 2011 and December 2020. Subjects were divided into two groups by age of onset symptoms, 1) EOS with onset between 13- to 18-years-old, and 2) VEOS with onset before 13-years-old. Descriptive statistics in term of frequency and percentage were used to describe clinical characteristics. Regarding the comparisons between groups, the differences were considered as statistically significant at the level of a p-value of less than 0.05.

Results: Forty-one participants were analyzed. The VEOS subgroup included nine participants (22%) and EOS subgroup included 32 participants (78%). The age of symptom onset ranged from 7.9 to 17.7 years old, with a mean of 14.2 years old (SD 2.5 years). The diagnostic stability was 82.9%. Thirty-seven (90.2%) and 39 participants (95.1%) demonstrated delusion and auditory hallucination, respectively. Only 13 participants (31.7%) reported visual hallucination. Moreover, there were statistically significant differences between EOS and VEOS on gender, other psychiatric comorbidities apart from depressive disorders, and the number of other psychotropic medication classes apart from antipsychotic medications. The female predominance demonstrated in VEOS subgroup, while the male predominance was found in EOS subgroup.

Conclusion: Although EOS was rare, the diagnostic stability of EOS was high. Auditory hallucination was the most common psychotic presentation reported in this population. The female predominance was demonstrated in the VEOS subgroup, while the male predominance was found in the EOS subgroup.

Keywords: Early-onset schizophrenia; Childhood; Adolescence; Clinical presentations

Received 7 November 2022 | Revised 26 December 2022 | Accepted 3 January 2023

J Med Assoc Thai 2023;106(2):172-9

Website: <http://www.jmatonline.com>

Schizophrenia is a chronic and severe psychiatric disorder that affects patients' behaviors, thought processes, perceptions, and emotional expression. Therefore, it can cause significant disability and distressing to patients and their families^(1,2). In adulthood, its lifetime prevalence appears to be about 1%⁽¹⁾ and the age of onset often starts in late adolescence or young adults with the incidence peaks in the early twenties⁽²⁾. However, schizophrenia in children and adolescents is very rare^(3,4). Reported by the observations from the National Institutes

of Mental Health (NIMH) cohort, the incidence of childhood-onset schizophrenia is less than 0.04%⁽⁴⁾. In general, these conditions in children and adolescents were defined by two terms. First, early-onset schizophrenia (EOS) was defined by an onset of illness before the age of 18 years old. Second, the subgroup of very early-onset schizophrenia (VEOS), sometimes known as childhood-onset schizophrenia (COS), was defined by an onset of illness before the age of 13 years old^(5,6). In Thailand, the previous study in 2010 showed the prevalence of schizophrenia by the age of 15 to 24 years old was 7.1 per 1,000 in male and 4.4 per 1,000 in female⁽⁷⁾. However, a limited number of studies focused on EOS and VEOS.

According to several neuroimaging studies, EOS was viewed as a severe form of the disorder because the evidence demonstrated continuously developmental processes of brain abnormalities from childhood to adulthood^(4,6,8). For instance, the developmental trajectories study revealed the progression of cortical gray matter loss in COS was exaggerated when compared to matched healthy

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How to cite this article:

Poovichayasumlit C, Limsuwan N. Clinical Presentations of Early-Onset Schizophrenia: A 10-Year Retrospective Chart Review. *J Med Assoc Thai* 2023;106:172-9.

DOI: 10.35755/jmedassocthai.2023.02.13779

controls. In addition, this gray matter developmental pattern eventually mimics the pattern seen in adult-onset cases as the children become young adults⁽⁸⁾. Moreover, several studies focused on the interactions between genetic and environment risk factors, which were dominant explanations for the etiology of schizophrenia⁽⁹⁻¹¹⁾.

Focusing on clinical manifestations of VEOS, insidious onset is frequently reported. The common positive symptoms in childhood are auditory hallucinations. In contrast, visual and tactile hallucinations are rarely found. Delusions in VEOS are less complex than in adolescents. Negative symptoms are predominantly flat or inappropriate affect^(12,13). As a neurodevelopmental disorder, several studies reported that COS associated with several premorbid functioning such as lower IQ, cognitive delays, academic difficulties, social and communication difficulties, transient autistic symptoms, and having high co-occurring rate with other neurodevelopmental disorders such as autism spectrum disorder and intellectual disability^(3,6,12). In addition, Coulon et al.⁽⁵⁾ interestingly compared adult-onset schizophrenia (AOS) and EOS, and revealed that EOS, in particular VEOS, demonstrated longer duration of untreated psychosis (DUP) than AOS. Moreover, Biswas et al.⁽¹⁴⁾ found COS patients reported more somatic and obsessive symptoms than AOS patients. Several studies demonstrated that EOS and VEOS associated with more misdiagnosis, greater severity, and poorer prognosis than AOS^(5,6,15,16).

However, many challenges in diagnosis of schizophrenia in children and adolescents are facing clinical practitioners. Firstly, the developmental limitations of children in describing complex internal symptoms lead to poor descriptions of the symptoms. Secondly, psychotic experiences are common in childhood, and they can be normal phenomena in this developmental stage which need to be differentiated with pathologic symptoms in schizophrenia⁽³⁾. Finally, little knowledge regarding the manifestations of EOS is provided in clinical practice because of the relative rarity of the disorder in children and adolescents. Therefore, the present study aimed to collect and describe the clinical presentations of EOS in a clinical setting. In addition, the authors aimed to compare the clinical presentations of EOS and VEOS.

Materials and Methods

Subjects

Patients diagnosed with schizophrenia when they were under 18 years old were recruited. In

Thailand, the psychiatric classification system was clinically based on the Diagnostic and Statistical Manual of Mental Disorders (DSM). Routinely, the psychiatric diagnoses at Ramathibodi Hospital were made by child and adolescent psychiatrists or residents under supervision. All participants, both inpatients and outpatients, that received psychiatric treatments at Ramathibodi hospital, Bangkok, Thailand between January 2011 and December 2020 were included. Subjects were divided into two groups by age of onset. EOS referred to participants who had the age of onset at 13- to 18-years-old and VEOS referred to participants who had the age of onset before 13-years-old. Participants with incomplete data were excluded.

Study design

The present study was a retrospective chart review of participants diagnosed with schizophrenia when they were under 18 years old. The electronic medical record system was assessed to identify the participants based on ICD-10 diagnosis coding (F20). After a process of identification, the full medical records of the participants were reviewed. The data collection included demographic data, age at first psychiatric assessment, age of symptom onset, DUP, clinical manifestations such as characteristics of psychotic symptoms, diagnostic stability, previous psychiatric diagnoses, psychiatric comorbidities, family history of psychiatric disorders, and treatments.

Statistical analysis

Descriptive statistics in term of frequency and percentage were used to describe clinical characteristics. For continuous data such as age and number of medications were presented by using means and standard deviation (SD). The DUP and the number of hospitalizations were presented by using median and interquartile range (IQR). Comparisons between group were performed by using Pearson chi-square test or Fisher's exact test for categorical variables. Continuous variables were analyzed with t tests for normally distributed data and with independent-sample Mann-Whitney U test in case of non-normally distributed data. The differences were considered as statistically significant at the level of p-value less than 0.05. Data analysis were performed by PASW Statistics, version 18.0 (SPSS Inc., Chicago, IL, USA).

Ethical approval

The present study was approved by the Human

Research Ethics Committee, Faculty of Medicine, Ramathibodi Hospital, Mahidol University (COA. MURA2021/743) prior to access the patient medical records. In the present study, only two researchers had permission to review the patient information from the electronic medical record system.

Results

According to the electronic medical record system of Ramathibodi Hospital, 163 patients both inpatients and outpatients were diagnosed with F20 schizophrenia and met the age inclusion criteria. However, 68 records could not be found because the medical record system of Ramathibodi Hospital by default removed the records of patients who had not contacted the hospital for longer than five years. After reviewing the full medical records, 30 records had the wrong diagnostic coding in computerized medical database. Moreover, 14 records were excluded because of incomplete data and 10 records were found to be duplicated. Finally, the present study population were 41.

Basic characteristics

All 41 participants were Thai ethnicity and nationality. There were 24 male participants (58.5%) and 17 female participants (41.5%). The age at first psychiatric assessment ranged between 8.0 and 18.7 years old with a mean of 14.5 years old (SD 2.5 years). The age of symptom onset ranged between 7.9 and 17.7 years old with a mean of 14.2 years (SD 2.5 years). The DUP, which is defined as the median time from the first episode of psychotic symptoms to the first psychiatric treatment was 3.0 (IQR 8.0) months (Table 1).

Clinical presentations of all participants

Thirty-seven (90.2%) and 39 participants (95.1%) demonstrated delusion and auditory hallucination, respectively. Only 13 participants (31.7%) reported visual hallucination. In addition, 22 participants (53.7%) showed mild disorganized behaviors such as talking or laughing without appropriate stimuli. In contrast, 12 participants (29.3%) demonstrated severe disorganized behaviors such as wandering, meditation in public places, biting others, and two participants (4.9%) had life-threatening catatonic behaviors. In addition, 27 participants (65.9%) demonstrated negative symptoms, which were mostly restricted affect.

Regarding non-psychotic symptoms, 12 participants (29.3%) reported obsessive-compulsive

symptoms. In addition, 85.4% showed mood symptoms, which were irritable (61%), depressed mood (41.5%), and anxious mood (29.3%). On the other hand, the authors found only four participants (9.8%) that demonstrated manic/hypomanic symptoms. Moreover, lifetime suicidal ideation was reported in 16 participants (39%). Four participants (9.8%) revealed at least one suicidal attempt but none of them had completed suicide. The number of suicidal attempts ranged from 0 to 2 times. Three-fourths of the participants who attempted suicide performed under the influence of psychotic symptoms such as voice command. On the other hand, one-fourth performed suicidal attempts under the influence of depressive mood.

Diagnostic stability

In the present study, the mean (\pm SD) length of follow up was 7.3 ± 4.5 years with range 1.9 to 20.6 years. The diagnostic stability of all participants was 82.9%. Thirty-four participants retained the original diagnosis as schizophrenia. In contrast, seven participants (17.1%) demonstrated unstable diagnoses (Table 2). However, all of 7 participants were finally changed their diagnoses back to schizophrenia.

In addition, 18 participants (43.9%) were diagnosed with other psychiatric diagnoses before schizophrenia. The most common previous diagnosis ($n=10$, 24.4%) was the group of other psychotic disorders such as unspecified psychotic disorder, brief psychotic disorder, and psychotic disorder due to medical condition. Respectively, other previous diagnoses were depressive disorders ($n=5$, 12.2%), obsessive compulsive disorder ($n=4$, 9.8%), and autism spectrum disorder ($n=4$, 9.8%). Some participants received more than one previous diagnosis before schizophrenia.

Treatments

Regarding inpatient treatments, 24 of 41 participants (58.5%) were hospitalized. The number of hospitalizations ranged from 0 to 11 admissions and the median (IQR) was 1.0 (3.0). Moreover, the mean (\pm SD) of current antipsychotics was 1.4 ± 0.9 . In addition, the mean (\pm SD) of previous antipsychotics was 4.1 ± 2.2 . The mean (\pm SD) of other psychotropic medication classes apart from antipsychotic medications, such as antidepressants, anxiolytics, and mood stabilizers, was 2.6 ± 1.0 . Twenty participants (48.8%) had lifetime history of Clozapine prescription. Moreover, eight participants (19.5%) received long-acting injectable anti-

Table 1. Clinical characteristics, diagnostic stability, comorbidities, and treatments

	All participants (n=41)	VEOS (n=9) (22.0%)	EOS (n=32) (78.0%)	p-value
Basic characteristics				
Sex; n (%)				0.021
• Male	24 (58.5)	2 (22.2)	22 (68.8)	
• Female	17 (41.5)	7 (77.8)	10 (31.2)	
Characteristics of age (years); mean±SD				
Age at first psychiatric assessment	14.5±2.5	11.4±2.0	15.5±1.9	<0.001
Age of onset	14.2±2.5	11.0±1.9	15.1±1.9	<0.001
Duration of untreated psychosis (months); median (IQR)	3.0 (8.0)	3.0 (5.5)	3.0 (11.0)	0.868
Clinical presentations				
Psychotic symptoms; n (%)				
• Delusion	37 (90.2)	7 (77.8)	30 (93.8)	0.204
• Auditory hallucination	39 (95.1)	9 (100)	30 (93.8)	1
• Visual hallucination	13 (31.7)	5 (55.6)	8 (25.0)	0.113
• Disorganized behaviors				0.411
Mild form	22 (53.7)	6 (66.7)	16 (50.0)	
Severe form	12 (29.3)	3 (33.3)	9 (28.1)	
• Negative symptoms	27 (65.9)	8 (88.9)	19 (59.4)	0.318
Mood symptoms; n (%)				
• Irritable	25 (61.0)	7 (77.8)	18 (56.3)	0.441
• Depressed	17 (41.5)	5 (55.6)	12 (37.5)	0.450
• Anxious	12 (29.3)	3 (33.3)	9 (28.1)	0.755
• Manic/hypomanic	4 (9.8)	2 (22.2)	2 (6.3)	0.204
Aggressive behaviors/hostility; n (%)	20 (48.8)	6 (66.7)	14 (43.8)	0.277
Obsessive-compulsive symptoms; n (%)	12 (29.3)	2 (22.2)	10 (31.3)	0.702
Lifetime suicidality; n (%)				
Suicidal ideation	16 (39.0)	5 (55.6)	11 (34.4)	0.276
Suicidal attempt	4 (9.8)	2 (22.2)	2 (6.3)	0.204
Number of hospitalizations; median (IQR)	1.0 (3.0)	3.0 (3.0)	1.0 (3.0)	0.137
Residual symptoms; n (%)				
Mild form of positive symptoms	11 (26.8)	4 (44.4)	7 (21.9)	
Severe form of positive symptoms	8 (19.5)	1 (11.1)	7 (21.9)	
Negative symptoms	5 (12.2)	0 (0.0)	5 (15.6)	
Positive and negative symptoms	3 (7.3)	0 (0.0)	3 (9.4)	
Family history of psychiatric disorders; n (%)	22 (53.7)	5 (55.6)	17 (53.1)	1
Diagnostic stability; n (%)				
Previous psychiatric diagnosis	18 (43.9)	4 (44.4)	14 (43.8)	1
Other psychotic disorders*	10 (24.4)	4 (44.4)	6 (18.8)	0.125
Mood disorders**	5 (12.2)	1 (11.1)	4 (12.5)	0.148
Obsessive-compulsive disorder	4 (9.8)	1 (11.1)	3 (9.4)	1
Autism spectrum disorder	4 (9.8)	0 (0.0)	4 (12.5)	0.559
Psychiatric comorbidities; n (%)				
Depressive disorders	7 (17.1)	0 (0.0)	7 (21.9)	0.315
Others***	11 (26.8)	5 (55.6)	6 (18.8)	0.048
Treatments				
Number of current antipsychotics; mean±SD	1.4±0.9	1.4±0.5	1.4±0.9	0.485
Number of previous antipsychotics; mean±SD	4.1±2.2	4.2±1.6	4.0±2.3	0.818
Number of other psychotropic medication classes; mean±SD	2.6±1.0	3.1±0.6	2.5±1.1	0.029
Clozapine; n (%)	20 (48.8)	6 (66.7)	14 (43.8)	0.277
Long-acting antipsychotic injection; n (%)	8 (19.5)	0 (0.0)	8 (25.0)	0.164
Electroconvulsive therapy; n (%)	4 (9.8)	0 (0.0)	4 (12.5)	0.559

VEOS=very early-onset schizophrenia; EOS=early-onset schizophrenia; SD=standard deviation; IQR=interquartile range

* i.e., unspecified schizophrenia spectrum and other psychotic disorders, brief psychotic disorder, schizoaffective disorder, psychotic disorders due to another medical conditions, substance-induced psychotic disorders; ** depressive disorders and bipolar disorders; *** i.e., intellectual disability, bulimia nervosa, binge-eating disorder, social anxiety disorder, acute stress disorder, trichotillomania

Table 2. Diagnostic instability (n=7)

Order	Unstable diagnoses
1.	Early-onset schizophrenia → schizoaffective disorder → early-onset schizophrenia
2.	Early-onset schizophrenia → schizoaffective disorder → early-onset schizophrenia
3.	Obsessive-compulsive disorder → early-onset schizophrenia → schizoaffective disorder → early-onset schizophrenia
4.	Early-onset schizophrenia → autism spectrum disorder → obsessive-compulsive disorder → autism spectrum disorder → early-onset schizophrenia
5.	Obsessive-compulsive disorder → early-onset schizophrenia → unspecified psychotic disorder → obsessive-compulsive disorder → early-onset schizophrenia
6.	Unspecified psychotic disorder → bipolar disorder → very early-onset schizophrenia → unspecified psychotic disorder → very early-onset schizophrenia
7.	Early-onset schizophrenia → psychotic disorder due to other medical condition → early-onset schizophrenia

psychotics for a period of time, and four participants (9.8%) participated in electroconvulsive therapy.

The comparison between VEOS and EOS

A sample of 41 participants were divided into two groups (VEOS and EOS). The VEOS subgroup (n=9, 22%) and EOS subgroup (n=32, 78%). They were compared in term of clinical characteristics (Table 1). There were statistically significant differences between EOS and VEOS in terms of gender, other psychiatric comorbidities apart from depressive disorders, and the number of other psychotropic medication classes apart from antipsychotic medications. Regarding the gender difference between the two groups, there were two male participants (22.2%) and seven female participants (77.8%) in the VEOS subgroup. There were 22 male participants (68.8%) and 10 female participants (31.2%) in EOS subgroup. As a result, this gender ratio was significantly different ($p=0.021$). The female predominance was demonstrated in VEOS subgroup, and a male predominance was observed in EOS subgroup. In addition, 55.6% of VEOS participants had other psychiatric comorbidities apart from depressive disorders such as intellectual disability, bulimia nervosa, binge-eating disorder, social anxiety disorder, acute stress disorder, and trichotillomania. In contrast, only 18.8% of EOS participants had other psychiatric comorbidities apart from depressive disorders. Moreover, the number of other psychotropic medication classes apart from antipsychotic medications, such as antidepressants, anxiolytics, mood stabilizers was statistically significant different between the two groups. In VEOS group, it was reported 3.1 ± 0.6 classes compared to 2.5 ± 1.1 classes in EOS group ($p=0.029$) (Table 1).

Discussion

The present study included nine VEOS participants (22%) and 32 EOS participants (78%).

The result revealed the diagnostic stability of schizophrenia in children and adolescents was high at 82.9%. Auditory hallucination was the most common psychotic presentation reported in this population. Moreover, there were statistically significant differences between EOS and VEOS on gender, other psychiatric comorbidities apart from depressive disorders, and the number of other psychotropic medication classes apart from antipsychotic medications. The female predominance was demonstrated in the VEOS subgroup while the male predominance was found in the EOS subgroup.

Regarding psychotic presentations the result showed that most of participants had auditory hallucination (95.1%) and delusion (90.2%). Congruently, most studies demonstrated that auditory hallucination dominantly presented in this population. David et al.⁽¹⁷⁾ revealed that 95% of 117 COS patients with a mean age of 13.6 years old had auditory hallucinations, which often were a part of reasons for referral. In addition, Masi et al.⁽¹³⁾ reviewed several studies regarding schizophrenia in children and revealed that auditory hallucination was found in 80% to 100% of patients and was the most common manifestation in this population. Interestingly, David et al.⁽¹⁷⁾ found visual hallucination in 80.3% of COS population and revealed that the presence of visual hallucinations indicated greater severity of illness, demonstrated by the earlier age of psychosis onset, younger age at assessment, lower IQ scores and lower Children's Global Assessment Scale (CGAS) scores. In contrast, the present study demonstrated that only 31.7% of all participants reported visual hallucination as clinical presentations. However, visual hallucination was found in 55.6% of VEOS subgroup compared to only 25% in EOS subgroup of the present study. Therefore, it is possible that visual hallucination tends to be found in younger groups of schizophrenia.

Recently, most studies demonstrated high diagnostic stability of schizophrenia in children and

adolescents. For instance, Kang et al.⁽¹⁸⁾ conducted a three-year follow-up study in China that included 101 EOS patients with the mean age of first onset of psychosis at 14.3 years old. The results revealed a diagnostic stability in 91.1% of participants. In addition, Xu et al.⁽¹⁵⁾ reported that the diagnostic stability of EOS was 76% in 65 Chinese subjects who were hospitalized and the mean length of follow up was 10.4 years. Moreover, Rad et al.⁽¹⁹⁾ conducted the study of psychotic-related disorders in children and adolescents in Romania and reported that 80.9% of 115 subjects maintained a diagnosis of psychotic spectrum disorder into adulthood. The subgroup of subjects who had onset before 13 years old reported their diagnoses were maintained in 82.4% and the subjects with onset after the age of 13 years showed 80.6% maintained in their diagnoses. However, this study included not only schizophrenia, but also brief psychotic disorder, severe depressive episode with psychotic symptoms, and psychotic mania. In Thailand, the previous study by Suwanno and Soongprasit⁽²⁰⁾ demonstrated that the diagnostic stability of 40 EOS patients was 90% with the mean of follow up period at 4.2 years. The present study similarly found high diagnostic stability (82.9%). Moreover, the authors found slightly higher diagnostic stability in VEOS subgroup than EOS subgroup (88.9% versus 81.3%). However, this difference did not reach the level of statistical significance. Eventually, high diagnostic stability of EOS reflected the continuous course of illness from childhood and adolescent to adulthood. However, it is important to highlight that the length of follow up period might directly affect the diagnostic stability.

Gender differences in schizophrenia was widely reported. Several studies indicated the incidence of schizophrenia is higher in men, especially in youth adults^(1,2,21). The central explanation of this issue was around the hormone hypotheses⁽²²⁾. Estrogens were proposed as neuroprotective hormone explained by several mechanisms as activation of estrogen receptor promotes gene expression of neuroprotective growth factors^(23,24). Classically, the dopamine hypothesis of schizophrenia proposed that hyperactivity of dopamine transmission is responsible for the positive symptoms in schizophrenia⁽¹⁾. Focusing on the relationship between estrogens and dopamine, dopaminergic functions is regulated by estrogens in several ways^(23,25) as estrogens increase dopamine sensitivity of dopamine D2/D3 receptors in the ventral tegmental area (VTA), which can decrease psychotic symptoms. Moreover, estrogen deficiency can lead

to increase Catechol-O-methyltransferase (COMT) activity and finally causes decline of dopaminergic functioning⁽²³⁾. In fact, estrogen deficiency was associated with increase psychotic symptoms in both genders^(23,25). Focusing on VEOS, this study found female predominance demonstrated in the VEOS subgroup and male predominance was found in the EOS subgroup. In females, low estrogens level in prepubertal stage might explain the higher prevalence of VEOS, as well as, the second peak of onset in female adults aged 45 to 50 years, which associated with menopause. In summary, age of symptom onset in schizophrenia was believed to relate with gonadal hormones^(22,23,25). However, the population of VEOS in the present study was very small (n=9). As a result, the female predominance in VEOS is still inconclusive.

The present study by retrospective design collected that already existed and patient-centered data in medical record system, which was appropriate for the very rare condition as EOS. In addition, the present study divided schizophrenia in child and adolescent populations into two groups, EOS and VEOS, and compared these different populations. However, the present study had limitations. Firstly, a small sample size was included in this study because of incomplete data, incorrect diagnosis coding, and the medical record system which removed the records of patients who had not contacted the hospital for longer than five years. Although, the authors performed a 10-year review, there was only 41 subjects recruited in the present study. As a result, the true difference in clinical presentations between EOS and VEOS group might be limited by Type II errors. Secondly, the psychiatric diagnoses in the present study were not based on structured clinical interviews and standardized assessments, which potentially were more reliable than clinical interviews. Finally, the study was limited to obtain some details of symptoms or clinical presentations because of the study design of chart reviewing.

Conclusion

Although EOS was rare, the diagnostic stability of EOS was high at 82.9%. Auditory hallucination was the most common psychotic presentation reported in this population. The female predominance demonstrated in the VEOS subgroup while the male predominance was found in the EOS subgroup.

What is already known on this topic?

As a neurodevelopmental disorder, EOS associated with premorbid functioning such as

lower IQ, cognitive delays, academic difficulties, social and communication difficulties, transient autistic symptoms, and having high co-occurring rate with other neurodevelopmental disorders. Focusing on clinical manifestations of VEOS, insidious onset is frequently reported. The common positive symptoms in childhood are auditory hallucination. In contrast, visual and tactile hallucinations are rarely found. In addition, EOS demonstrated longer DUP than AOS.

What this study adds?

This study divided schizophrenia in child and adolescent populations into two groups, EOS and VEOS, and compared these different populations. This study found statistically significant differences between EOS and VEOS on gender, other psychiatric comorbidities apart from depressive disorders, and the number of other psychotropic medication classes apart from antipsychotic medications. Interestingly, the female predominance was demonstrated in the VEOS subgroup while the male predominance was found in the EOS subgroup. Although, gender differences in adult schizophrenia were widely reported, the results regarding this issue in child and adolescent population have been inconsistent.

Conflicts of interest

The authors declare no conflict of interest.

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