ลักษณะทางคลินิกของผู้ป่วยโรคจิตเภทในวัยรุ่นในสถาบันจิตเวชศาสตร์สมเด็จเจ้าพระยา

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**โรงพยาบาลยุวประสาทไวทโยปถัมภ์*
***สถาบันจิตเวชศาสตร์สมเด็จเจ้าพระยา*

บทคัดย่อ

วัตถุประสงค์ โรคจิตเภทเป็นโรคทางจิตเวชที่ส่งผลกระทบต่อการดำเนินชีวิต โรคจิตเภทในเด็กและวัยรุ่นจัดอยู่ในกลุ่มโรคความผิดปกติจากการพัฒนาระบบประสาท และมักสัมพันธ์กับความรุนแรงที่มากกว่า รวมถึงพยากรณ์โรคไม่ดี การศึกษาครั้งนี้มีวัตถุประสงค์เพื่อสำรวจลักษณะทางคลินิกของโรคจิตเภทในกลุ่มวัยรุ่นอายุระหว่าง 14 - 18 ปี ที่เข้ารับการรักษา ณ โรงพยาบาลจิตเวชระดับเหนือศูนย์ตติยภูมิในกรุงเทพมหานคร รวมทั้งศึกษาความสัมพันธ์ระหว่างกลุ่มผู้ป่วยที่มีอาการคงที่กับกลุ่มที่มีอาการรุนแรงกับตัวแปรทางคลินิกต่างๆ

วิธีการศึกษา เป็นการศึกษาเชิงพรรณนาแบบย้อนหลัง โดยเก็บข้อมูลจากผู้ป่วยวัยรุ่นทุกคนตั้งแต่อายุ 14 - 18 ปี ที่ได้รับการวินิจฉัยเป็นโรคจิตเภทเป็นครั้งแรกระหว่างปี พ.ศ. 2561 จนถึงปี พ.ศ. 2566 ในสถาบันจิตเวชศาสตร์สมเด็จเจ้าพระยา วิเคราะห์ข้อมูลทั่วไปโดยใช้สถิติเชิงพรรณนา และวิเคราะห์หาความสัมพันธ์ระหว่างตัวแปรกลุ่มที่อาการคงที่และรุนแรงโดยใช้สถิติแบบ Chi-square test หรือ Fisher's exact test และประมาณค่า Odds Ratio ด้วยวิธีการถดถอยโลจิสติกแบบตัวแปรเดียว

ผลการศึกษา กลุ่มตัวอย่างในการศึกษานี้มีจำนวนทั้งหมด 96 คน กลุ่มประชากรศึกษาส่วนใหญ่เป็นเพศชาย คิดเป็นร้อยละ 75 และมีอายุเฉลี่ยเท่ากับ 16.8 ปี โรควินิจฉัยร่วมที่พบบ่อยที่สุดคือ ความผิดปกติของการใช้สารเสพติด คิดเป็นร้อยละ 36.6 โดยสารเสพติดที่ใช้มากที่สุดคือกัญชา นอกจากนี้ผู้ที่ได้รับการวินิจฉัยว่าเป็นโรคจิตเภทพบว่าได้รับการวินิจฉัยเป็นโรคทางจิตเวชอื่นมาก่อนถึงร้อยละ 54.2 โดยโรคที่พบมากที่สุดคือโรคจิตที่เกิดจากการเสพสารเสพติดมากที่สุด อย่างไรก็ตาม ไม่พบความสัมพันธ์ที่มีนัยสำคัญทางสถิติระหว่างตัวแปรที่ศึกษาและความรุนแรงของโรค (เปรียบเทียบระหว่างกลุ่มที่มีอาการคงที่กับกลุ่มที่มีอาการรุนแรง)

สรุป ผู้ป่วยโรคจิตเภทเด็กและวัยรุ่นมักพบบ่อยในเพศชายและพบอัตราการใช้สารเสพติดสูง ผลการวิจัยชี้ให้เห็นถึงความสำคัญในการป้องกันการใช้สารเสพติดในประเทศไทย อาการนำที่พบก่อนวินิจฉัยโรคจิตเภทที่พบบ่อยที่สุดคือการเปลี่ยนแปลงด้านพฤติกรรม ข้อมูลนี้อาจมีประโยชน์ในการค้นหาผู้ป่วยในระยะแรกในอนาคต

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Exploring Clinical Features of Early Onset Schizophrenia at Somdet Chaopraya Institute of Psychiatry

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ABSTRACT

Objective: Schizophrenia is a major psychiatric disorder that causes significant functional impairment. When onset occur in childhood or adolescence, it is considered a neurodevelopmental disorder and is associated with greater severity and poor prognosis. This study investigates the clinical features of schizophrenia in adolescents aged 14 to 18 years at the supra-tertiary psychiatric hospital in Bangkok and association between stable versus severe group and clinical variables.

Methods: In a descriptive retrospective study (N = 96), all patients aged 14 to 18 years who received the first diagnosis of schizophrenia at Somdet Chaophraya Psychiatric Institute between 2018 and 2023 were included in the study. Descriptive statistics were used to characterize the sample. Associations between clinical factors and illness severity were analyzed using chi-square or Fisher's exact tests, and odds ratio (OR) were estimated using univariable logistic regression.

Results: The study included 96 participants who met the inclusion criteria. Among these, 75% were male, with a mean age diagnosis of 16.8 years. Comorbidities were present in 36.6% of the cases, with substance use disorder being the most prevalent. Among this cannabis users were the most frequently reported. Prior to the schizophrenia diagnosis, 54.2% of participants had been diagnosed with other mental health conditions, most frequently substance-induced psychosis. However, no statistically significant associations were observed between the study variables and illness severity (stable vs. severe groups).

Conclusion: Early onset schizophrenia was characterized by predominance of male patients with high rate of comorbid substance use. These findings highlight the importance of substance use prevention policy in Thailand. Behavioral changes were the most common prodromal manifestation, and this information may contribute to earlier detection of the disorder.

Keyword: early onset schizophrenia, adolescent onset schizophrenia, psychosis, childhood, adolescent

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INTRODUCTION

Schizophrenia: Clinical Overview

Schizophrenia is a major psychiatric disorder that causes significant functional impairment worldwide. It is recognized as one of the twenty-five leading causes of disability.[1] Schizophrenia often originates in early life and exerts long term consequences, particularly in term of hospitalization and rehabilitation costs. Data indicate that healthcare expenditure of schizophrenia patients in the United States is greater than that of patients with cancer.[1] Schizophrenia has a significant impact on patients, their families and society. Given its early onset and chronic trajectory, schizophrenia particularly in children and adolescents is increasingly understood as a neurodevelopmental disorder.[2] Schizophrenia in adolescents with psychotic symptoms onset before the age of 18 is specifically defined as early-onset schizophrenia, whereas childhood-onset schizophrenia refers to onset before the age of 13.[3]

The course of schizophrenia is divided in to four phases: premorbid phase, prodromal phase, active phase and chronic or residual phase.[4] A formal diagnosis is established during the active phase, as the clinical features are most obvious at this stage. The premorbid phase has only subtle cognitive, behavioral or social changes.[4] The prodromal phase follows, during which patients begin to exhibit nonspecific symptoms. The prodromal phase is often identified retrospectively once the disorder has progressed to the active phase and clinical history has reviewed.[4] The prodromal phase has been identified as a critical period for research, given its potential role in facilitating the early detection of schizophrenia. Yung et al. categorized prodromal symptoms into seven domains: neurotic symptoms, mood-related symptoms, changes in volition, cognitive changes, physical symptoms, other symptoms, and behavioral changes.[5] Clinical features of schizophrenia in active phase consist of positive and negative symptoms. Following the active phase, patients enter the chronic or residual phase.

The Landscape of Early-Onset Schizophrenia: Symptoms, Risk Factors, and Illness Severity

Although childhood-onset schizophrenia is very rare, with an incidence of only 0.04 percentages[6], evidence indicates that early and childhood-onset schizophrenia represent more severe forms of the disorders.[7] The clinical presentation of early-onset schizophrenia can be similar to that of adulthood-onset schizophrenia. However, some studies have found that early-onset schizophrenia is presented by greater disorganization and more characterized negative symptoms compared to adulthood-schizophrenia.[7] Childhood and early onset schizophrenia are correlated with greater illness severity, impaired peer relationship, academic difficulties, poor social skill and increase in brain abnormalities.[3] However, studies about schizophrenia in child and adolescent is less extensive than adulthood schizophrenia onset.

Parallel to these clinical features, the risk factors associated with early onset schizophrenia–categorized into environmental, psychosocial, and biological domains. Environmental risk factors include advanced paternal age[8], pregnancy complications[9-11], and cannabis use.[12-14] Cannabis use has been associated with a twofold increase in the risk of developing schizophrenia[12], with psychotic symptoms emerging approximately 2.7 years after initial exposure.[13] Regarding psychological risk factor, childhood trauma, including physical, sexual, and emotional abuse, and neglect has been implicated.[15] Finally, biological risk factors are primarily genetic.[16,17] Childhood onset schizophrenia has been reported to be more associated with genetic factor than adult-onset schizophrenia, with heritability estimates of up to 80 percentages.[3]

Defining Severity in the Thai Context

The interplay of these multifaceted risk factors not only influences disease onset but also dictates the clinical trajectory and severity of the disorder. In DSM-5TR, schizophrenia severity is conceptualized as a dimensional construct and is rated through quantitative assessment of core psychotic symptom domains, including delusions, hallucinations, disorganized speech, abnormal

psychomotor behavior, and negative symptoms, each graded on a 5-point severity scale.[18] Building on this dimensional approach, recent literature has proposed severity specifiers that extend beyond symptom intensity to include clinically meaningful outcomes such as hospitalization, reflecting greater illness burden and functional impairment.[19] Consistent with this framework, clinical practice guidelines, including those from the National Institute for Health and Care Excellence (NICE), indicate that electroconvulsive therapy (ECT) is reserved for severe presentations of schizophrenia, such as treatment-resistant illness, catatonia or severe symptom exacerbations.[20] Accordingly, in this study, the term severe schizophrenia was used to describe patients meeting at least one of the following criteria: (1) history of ECT (electroconvulsive therapy), (2) history of psychiatric hospitalization, or (3) presence of active or residual symptoms, including psychotic symptoms, irritable or elevated mood, or catatonia. Patients who did not meet any of these criteria and were clinically stable were classified as the non-severe (stable) group.

Rationale and Objectives

International literature consistently identifies early-onset schizophrenia (EOS) as a distinct, more severe neurodevelopmental phenotype of the disorder. Compared to adult-onset cases, EOS is characterized by a heavier symptom burden, diminished functional outcomes and increased treatment resistance and increase in brain abnormalities. Early-onset schizophrenia is presented by greater disorganization and more characterized negative symptoms compared to adulthood-schizophrenia.

In Thailand, research on schizophrenia in children and adolescents remain extremely limited. Previous Thai studies, conducted in university-based medical school hospitals, primarily described clinical presentations of EOS and very early-onset schizophrenia (VEOS) using small retrospective samples (approximately 40 patients). These studies reported that auditory hallucinations and delusions were the most common psychotic symptoms, with high diagnostic stability, and identified differences between EOS and VEOS in gender distribution and psychiatric comorbidities.[21] However, illness severity was not systematically examined using outcome-based measures, nor were clinical risk factors for severe disease courses explored.

In addition, differences in clinical settings may contribute to important knowledge gaps between university hospital and supra-tertiary psychiatric hospital. Supra-tertiary psychiatric hospitals function as specialized referral centers that manage high volume of complex and severe psychiatric cases. To address these gaps, the present study leveraged the resources of a supra-tertiary psychiatric hospital to investigate a larger cohort of adolescents with schizophrenia (N = 96).

The objectives of this study were (1) the clinical features of early onset schizophrenia and (2) to examine the association between stable versus severe schizophrenia group and specific clinical risk factors at the Somdet Chaophraya Psychiatric Institute which is the supra-tertiary psychiatric hospital in Bangkok, Thailand.

METHODS

Ethics approval

This retrospective study was approved by the Institutional Review Board of the Somdet Chaophraya Institute of Psychiatry (SD.IRB.APPROVAL 028/2567). Informed consent was waived due to the retrospective nature of the study and the use of de-identified data to ensure the confidentiality of participant information.

Participants

All patients who received first diagnosis of schizophrenia, determined by the date of the initial diagnosis according to ICD-10 criteria (International Classification of Disease and Related Health Problem 10th Revision; F20.0-F20.9), occurred between 2018 and 2023, at ages 14 to 18 at Somdet Chaophraya Psychiatric Institute were included. Exclusion criteria included the patient's medical record has been loss. Patients aged 13 years were excluded, as treatment at Somdet Chaophraya Psychiatric Institute is provided to patients

aged 14 years and older. A retrospective consecutive sampling method was applied by screening all electronic medical records that met the inclusion criteria during the study.

Study design

This study employed a retrospective observational descriptive design, analyzing data extracted from the medical records of patients diagnosed with the early-onset schizophrenia from Somdet Chaophraya Psychiatric Institute (supra-tertiary psychiatric hospital in Bangkok)

Data collection

A structured data collection form was developed based on prior literature and study objectives including patient's general characteristics, childhood history, family history, prodromal symptoms, current symptoms. After receiving ethical approval; the hospital information technology staff generated a list of eligible patient identification. All medical records were screened and abstracted by a single investigator to ensure consistency. Clinical data were extracted from medical record system and entered into a secured database without patient identifies.

Data analysis

The primary analysis consisted of descriptive statistics, including number, frequency, percentage, mean and standard deviation. The secondary analysis examined the association between stable versus severe group and clinical variables. The association between variables was evaluated using the chi-square test, while univariable logistic regression was utilized to determine the odds ratio (OR) with 95% confidence intervals. A P-value ≤ 0.05 was considered statistically significant. The severe group was defined as patients who met at least one of the following criteria: (1) a history of electroconvulsive therapy (ECT), (2) a history of psychiatric hospitalization, or (3) the presence of active or residual symptoms, including psychotic symptoms, irritable mood, elevate mood, or catatonia. The stable group was defined as stable in current symptoms were documented and did not meet any criteria for the severe group. In case of incomplete data, descriptive results were presented as percentages, with missing data reported separately. For chi-square analysis, missing data were handled using a Pairwise Deletion approach. All statistical analyses were performed using SPSS for Window (version 19.0).

RESULTS

Descriptive Characteristics of the Sample

Basic characteristic

A total of 131 patients were identified from the electronic medical record system using ICD-10 codes F20.0–F20.9. Following a detailed chart review, 31 patients were excluded because their final clinical diagnoses were inconsistent with schizophrenia. An additional four patients were excluded due to an age at diagnosis exceeding 18 years. This resulted in a final study sample of 96 patients. (Figure 1) The cohort was predominantly male (72 males [75%], 24 females [25%]), with a mean age of 16.8 years (SD = 1.17; range: 14 - 18 years). The prevalence of schizophrenia diagnoses was higher among older adolescents within the 14 - 18–year range. (Table 1)

Table 1 Demographic data of the Study Participants (N = 96)

Demographic	N (N = 96)	%
Gender		
Male	72	75
Female	24	25
Education level		
Primary education	18	20
Junior high school	39	43.3
Senior high school / Certificate of Technical Vocation	30	33.3
University (Bachelor's degree)	0	0
High Vocational Certificate	3	3.3
No information	6	6.2
Education/working status		
studying	37	44.6
working	3	3.6
Not studying or working	43	51.8
No information	13	13.5

Comorbid Psychiatric Diagnoses

Among the 96 patients, 35 (36.5%) had at least one psychiatric comorbidity. The most common comorbidity was substance use disorder (SUD) (n = 23, 58.9% of those with comorbidity), followed by intellectual disability (n = 4, 10.3%), autism spectrum disorder (n = 4, 10.3%), and depressive disorder (n = 4, 10.3%). Notably, 52 patients (54.2%) had a prior psychiatric diagnosis, with 38 (73.1% of those with prior psychiatric diagnosis) having one diagnosis, 11 (21.1%) two, and 3 (5.7%) three diagnoses. The most frequent prior diagnosis was substance-induced psychosis (n = 16, 23.2% of those with prior psychiatric diagnosis), followed by psychosis not otherwise specified (n = 13, 18.8%), autism spectrum disorder (n = 9, 13%) and major depressive disorder (n = 5, 7.2%). (Table 2)

Substance Use History

Forty-six patients (48.4%) reported a history of substance use. Among these, 10 (10.5%) used one substance, 21 (22.1%) used two, 12 (12.6%) used three, 2 (2.1%) used four, and 1 (1%) used five substances. The mean duration of substance use prior to diagnosis was 26.4 months (SD not reported; range: 1 - 84 months). Cannabis was the most commonly used substance (n = 28, 27.7% of the full sample), followed by alcohol (n = 24, 23.8%), stimulants including amphetamine and methamphetamine (n = 19, 18.8%), and kratom (n = 13, 12.9%).

Family Psychiatric History

Thirty patients (31.3%) reported a family history of psychiatric disorders. The most common familial condition was schizophrenia (n = 14, 41.2% of those with family history), followed by unspecified psychosis (n = 9, 26.5%) and other psychiatric disorders (n = 4, 11.8%). Of the patients with a family history of psychiatric disorders, half were found to have an affected first-degree relative, 41.2% had a second degree-relatives.

Clinical Features

The most commonly reported prodromal symptom was behavioral change (n = 24, 31.6%), followed by mood-related symptoms (n = 23, 30.2%). Substance-induced psychosis was the initial presentation in 22 patients (29%). Post-treatment outcomes, defined by clinical status at the most recent outpatient follow-up, revealed that 34.3% of patients continued to experience active or residual symptoms, including positive symptoms (n = 24, 25%), negative symptoms (n = 7, 7.3%), catatonia (n = 1, 1%), and anxiety (n = 1, 1%). Sixty patients (62.5%) had been hospitalized for psychiatric treatment.

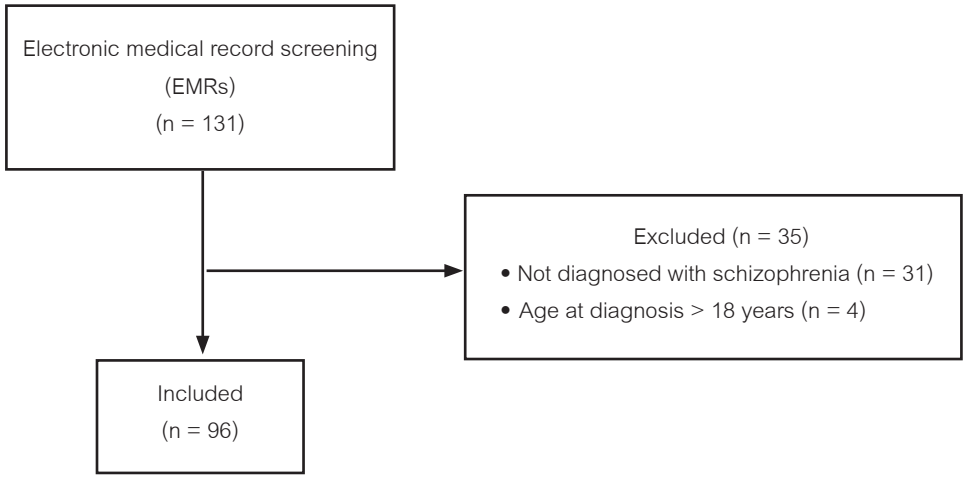


Figure 1 Flowchart of the study participant selection process. From an initial screening of 131 EMRs, 35 individuals were excluded based on diagnosis and age criteria, resulting in a final study population of 96 adolescents with schizophrenia.

Table 2 Baseline Clinical Characteristics of the Study Participants (N = 96)

Base line Clinical features	N (N = 96)	%
Comorbidity		
no	61	63.5
yes	35	36.5
1 diagnosis	31	88.6[a]
2 diagnoses	4	11.4[a]
Prior diagnosis		
no	44	45.8
yes	52	54.2
1 diagnosis	38	73.1[b]
2 diagnoses	11	21.1[b]
3 diagnoses	3	5.7[b]
Underlying medical conditions		
no	87	90.6
yes	9	9.4
1 underlying disease	7	77.8[c]
2 underlying diseases	2	22.2[c]
History of substance use		
no	49	51.6
yes	46	47.9
1 substance	10	10.5[d]
2 substances	21	22.1[d]
3 substances	12	12.6[d]
4 substances	2	2.1[d]
5 substances	1	1[d]
No information	1	1
Clinical features		
Prodromal symptoms		
1 symptom	64	66.7
2 symptoms	6	6.25
No information	26	28.1
Hospitalization history		
No (Outpatient treatment)	36	37.5
Yes	60	62.5
Current symptoms * Clinical status at the most recent outpatient follow-up		
Stable	61	63.5
Positive symptoms	24	25
Negative symptoms	7	7.3
Catatonia	1	1
Anxiety	1	1
No information	2	2

[a] Percentages based on n = 35 patients with comorbidity diagnosis
[b] Percentages based on n = 52 patients with previous diagnosis (excluding current schizophrenia)
[c] Percentages based on n = 9 patients with underlying diseases
[d] Percentages based on n = 95 patients with history of substance use

Comparison Between Stable and Severe Groups

Patients were classified into the severe if they met at least one of the following criteria: a history of electroconvulsive therapy (ECT), psychiatric hospitalization, or the presence of active or residual psychotic symptoms at the time of data collection. Comparative analysis between the two groups revealed statistically significant differences in the prevalence of certain comorbidities. Specifically, intellectual disability (ID) and attention-deficit/hyperactivity disorder (ADHD) were observed exclusively in the stable group (both 9.4%), whereas no cases were identified in the severe group ($p = 0.035$ for both comparisons). Although, overall substance use history did not differ significantly, a higher proportion of severe patients reported substance use compared to stable patients (54.0% vs 37.5%)

In contrast, no significant differences were found between the groups in terms of gender distribution ($p = 0.617$), overall comorbidity status ($p = 0.099$), or prior psychiatric diagnoses ($p = 0.148$). Family psychiatric history showed no meaningful variation between the groups ($p > 0.999$), and educational level, underlying medical conditions, and current occupational or educational status were also comparable (all $p > 0.05$). Collectively, these findings suggest that while neurodevelopmental disorders such as ID and ADHD are

more common among adolescents with stable illness trajectories, other demographic and clinical variables did not significantly differentiate between the two groups. (Table 3)

To future examine factors associated with symptom stability, univariable logistic regression was conducted, with result in Table 4. The analysis demonstrated that kratom use disorder was associated with severe illness, showing the highest odds ratio (OR = 7.294, 95% CI = 0.973 - 321.63). The small number of cases in this category contributes to significant model instability and limited precision for this estimate. Although non-significant association, the direction and magnitude of the OR suggest a potentially trend relationship between kratom exposure and severe clinical course. Comorbid substance use disorder in general showed an increased likelihood of instability (OR = 1.954, 95% CI = 0.754 - 5.161) but the association did not reach statistical significance (p = 0.129). Similarly, stimulant use demonstrated a non-significant trend toward higher odds of instability (OR = 2.350, 95% CI = 0.818 - 7.373, p = 0.0826). Regarding neurodevelopmental disorders, both intellectual disability (ID) and ADHD were observed exclusively within the stable group (9.4% in stable group vs. 0.0% in the severe group). Consequently, odds ratio and their corresponding 95% confidence intervals could not be reliably estimated due to the absence of these conditions in the stable cohort.

Overall, the univariable analysis showed that kratom use disorder was associated with a non-significant trend toward higher odds of clinical instability. Similarly, other substance use disorders and neurodevelopmental disorder demonstrated possible but non-significant associations with instability.

DISCUSSION

The present study observed a significantly higher prevalence of intellectual disability (ID) and attention-deficit/hyperactivity disorder (ADHD) within the stable group. However, these findings diverge from established literature, notably the research by Kessler et al., which reported that comorbid ID is typically associated with a marked increase in psychiatric hospitalizations, longer inpatient duration, and frequent emergency visits.[22] This discrepancy suggests a potential misclassification bias in the current study's categorization of stability. Despite these categorical inconsistencies, the overall prevalence of neurodevelopmental comorbidities in this cohort remains striking. Following substance use disorders, intellectual disability and autism spectrum disorder were identified as the second and third most frequent comorbidities, respectively. These findings highlight the frequent co-occurrence of neurodevelopmental disorders and early-onset schizophrenia. Nevertheless, further research is required to determine whether these comorbidities are definitively linked to increased illness severity. Future studies should employ standardized clinical instruments, such as the Positive and Negative Syndrome Scale (PANSS) or the Brief Psychiatric Rating Scale (BPRS), to provide a more objective and granular assessment of symptomatic severity.

Beyond neurodevelopment factors, prior research has demonstrated that substance use is associated with increased hospitalization and relapse risk in schizophrenia.[22] Although the present study did not find a statistically significant difference in overall substance use between the stable and severe groups, a higher proportion of severe patients reported substance use. Kratom use disorder was associated with a non-significant trend toward higher odds of clinical instability in univariable analysis; however, this association should be interpreted with caution due to potential confounding and the absence of multivariable adjustment. The wide confidence interval suggests low precision of the estimate, likely due to the small number of kratom users, and therefore the magnitude of the association should be interpreted carefully. This finding aligns with the study by Maxsaya Baez Nunea et al., which given emerging evidence that kratom may exacerbate psychiatric symptoms.[23] However, interpreting this association requires caution, as pattern of kratom consumption in Thailand frequently involve polysubstance mixtures. Users may consume boiled kratom alone, but it is common to mix kratom with cough syrup, tramadol, or

Table 3 Association between stable versus severe schizophrenia group and clinical variables

Factor	Patient numbers		p-value
	severe (%)	stable (%)	
Demographic (N = 96)			
gender			0.617[a]
male	47 (73.4)	25 (78.1)	
female	17 (26.6)	7 (21.9)	
Education level			0.652[b]
Primary education	14 (23.3)	4 (13.3)	
Junior high school	26 (43.3)	13 (43.3)	
Senior high school / Certificate of Technical Vocation	18 (30.0)	12 (40.0)	
High Vocational Verification	2 (3.3)	1 (3.3)	
Education / working status			0.161[b]
Not studying / working	31 (56.4)	12 (42.9)	
Studying	21 (38.2)	16 (57.1)	
Working	3 (5.5)	0 (0.0)	
Comorbidity (N = 96)			
Autism spectrum disorder			>0.999[b]
no	62 (96.9)	31 (96.9)	
yes	2 (3.1)	1 (3.1)	
Intellectual disability			0.035[b]*
no	64 (100.0)	29 (90.6)	
yes	0 (0.0)	3 (9.4)	
ADHD			0.035[b]*
no	64 (100.0)	29 (90.6)	
yes	0 (0.0)	3 (9.4)	
Specific learning disorder			0.551[b]
no	62 (96.9)	32 (100.0)	
yes	2 (3.1)	0 (0.0)	
Substance use disorder (N = 95)			
Cannabis			0.209[a]
no	37 (58.7)	23 (71.9)	
yes	26 (41.3)	9 (28.1)	
Stimulant			0.083[a]
no	38 (60.3)	25 (78.1)	
yes	25 (39.7)	7 (21.9)	
Kratom			0.033[a]*
no	51 (81.0)	31 (96.9)	
yes	12 (19.0)	1 (3.1)	
Family psychiatric disorder			>0.999[b]
no	39 (69.6)	18 (69.2)	
yes	17 (30.4)	8 (30.8)	

Note: Data are presented as n (%). [a] Chi-square test; [b] Fisher's exact test. Fisher's exact test was used when expected cell counts were < 5. Statistically significant at $p \leq 0.05$.

Table 4 Univariable analysis of factors associated with symptom stability in adolescents with schizophrenia

Variable	OR (95% CI)	p-value
Comorbid substance	1.954 (0.754 - 5.161)	0.129
Kratom	7.294 (0.973 - 321.63)	- *
Stimulant	2.350 (0.818 - 7.373)	0.083
Cannabis	1.796 (0.661 - 5.129)	0.210

* Odds ratios and 95% confidence intervals were derived from univariable logistic regression models. Due to sparse data and small cell counts, p-values for some variables were not reported and are discussed in the Discussion section.

sweetened soft drinks to enhance psychoactive effects or improve taste. Importantly, individuals typically report only "kratom use" without disclosing co-ingested substances, making it difficult to determine the specific contribution of kratom itself to clinical instability. Given the high prevalence of kratom-associated polysubstance mixtures in Thailand, the observed association may partially represent the impact of multi-drug exposure rather than kratom alone. This limitation underscores the need for future research to differentiate between pure kratom exposure and kratom-associated polysubstance use when evaluating psychiatric outcomes in adolescents with schizophrenia.

Regarding substance use more broadly, cannabis was the most commonly used substance in this study. Linda et al. reported that cannabis use increases the risk of relapse among individuals with schizophrenia.[24] In addition, Large M et al. reported that cannabis use is associated with the development of psychotic symptoms approximately 2.7 years after initial exposure.13 In our sample, with cannabis being the most commonly used substance, followed by methamphetamine and kratom. The mean duration of substance use prior to the onset of schizophrenia was approximately 2.2 years. However, in Thailand, adolescent substance use behavior is often characterized by the use of multiple substances, which complicates the interpretation of substance-specific effects on illness stability.

These finding underscore the critical importance of strengthening substance-use prevention policies in Thailand. The 2022 liberalization of cannabis laws, which allowed purchase and sale without medical prescription. However, in 2025, Thailand began reinstating stricter controls, requiring medical prescriptions for cannabis used for medical treatment. Similarly, kratom was removed from the list of prohibited substances in 2021. Although the legislation outlines conditions for possession and sale, regulatory loopholes have made kratom widely accessible to general population.

Moreover, previous evidence has indicated that childhood and early onset schizophrenia are correlated with greater illness severity. Specifically, meta-analytic data from 10 studies have demonstrated a statistically significant relationship between an earlier age at onset and poorer hospitalization outcomes, suggesting that these patients often experience more frequent or prolonged hospitalizations. Furthermore, a lower age at onset has been linked to more pronounced negative symptoms.[25] In line with this study, the rate of psychiatric hospitalization in our sample was relatively high (62.5%), and approximately 35% of patients continued to have residual psychotic symptoms at the time of data collection, emphasizing the chronic and relapsing nature of schizophrenia in adolescence. These findings underline the importance of early detection, continuous monitoring, and integrated treatment approaches that address both psychotic symptoms and comorbid conditions such as substance use disorders

Compared to prior Thai studies with smaller cohorts (N≈40), this study provides a substantially larger sample, enabling more reliable characterization of adolescent-onset schizophrenia in Thailand. However, this study has several limitations. First, this study is limited by its retrospective design, missing prodromal data in nearly one-third of cases, and reliance on univariable analysis without controlling for confounders. These limitations warrant cautious interpretation of the observed associations. Second, substance use history relied on medical records and patient report, which may be subject

to underreporting. Third, the retrospective design may have introduced measurement bias, selective bias and referral bias may be present as the sample was drawn from a tertiary care hospital where more severe and complex cases are more likely to be represented. In addition, misclassification may have occurred in the categorization of severe patients, as this grouping was conducted post hoc analysis. The retrospective data only recorded whether patients had a history of hospitalization, without specifying duration for example rehospitalization in 12 months. Future prospective studies with systematic toxicology testing are needed to disentangle pure kratom exposure from polysubstance mixtures and to determine whether the associations observed here persist after multivariable adjustment and are warranted to clarify the causal relationship between substance use and illness trajectory in adolescent schizophrenia.

CONCLUSION

Schizophrenia in adolescents were characterized by predominance of male patients with high rate of comorbid substance use. These findings highlight the importance of substance use prevention policy in Thailand. Behavioral changes were the most common prodromal manifestation, and this information may contribute to earlier detection of the disorder. The rate of psychiatric hospitalization was relatively high and many patients continued to have residual psychotic symptoms. This emphasizing the chronic and relapsing nature of schizophrenia in adolescence. Clinically, the findings highlight the need for routine screening of kratom and polysubstance use among adolescents presenting with early psychotic symptoms, as well as enhanced monitoring for patients with neurodevelopmental disorders.

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Conflict of Interest

The authors declare that they have no competing interests.

Ethical Approval

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was granted by Institutional Review Board of the Somdet Chaophraya Institute of Psychiatry at the Somdet Chaophraya Psychiatric Institute, Bangkok, Thailand.

Authors' Contributions

Chananya Suksawatt: Conceptualization, methodology, data curation, formal analysis, and writing – original draft preparation.; Buranat Runglaksameesri: Conceptualization, formal analysis, and writing – review and editing.; Sutha Supanya: Conceptualization, and writing – review and editing.; Janyaporn Jiamjaroenkul: Conceptualization, and writing – review and editing.

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