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Comparative Clinical and Sociodemographic Assessment of Substance Use in First Episode, Drug-naïve Psychosis and Schizophrenia Patients

İlk Atak, İlaç Kullanmamış Psikoz ve Şizofreni Hastalarında Madde Kullanımının Karşılaştırmalı Klinik ve Sosyodemografik Analizi

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Abstract

Objective: This study aims to compare recent-onset, drug-naïve patients with first-episode psychosis (FEP) and patients with schizophrenia in terms of substance and smoking history, and to explore their associations with sociodemographic and clinical characteristics.

Methods: A total of 107 patients were included: 56 with drug-naïve FEP and 51 with schizophrenia. Standardized clinical instruments were used, including the Clinical Global Impression–Severity Scale (CGI-S), the Scale for the Assessment of Negative Symptoms (SANS), the Scale for the Assessment of Positive Symptoms (SAPS), and the Calgary Depression Scale for Schizophrenia (CDSS).

Results: Substance use was more prevalent among schizophrenia patients (41.2%) compared to FEP patients (25.0%). In both groups, substance use was associated with increased smoking, alcohol consumption, and greater clinical severity. Specifically, FEP patients with substance use reported significantly higher depressive and negative symptoms, as well as greater illness severity. Among schizophrenia patients, substance use was correlated with elevated SAPS, SANS, and CGI-S scores, as well as higher rates of self-mutilation.

Conclusion: Substance use contributes to greater symptom burden, behavioral dysregulation, and overall clinical severity in both FEP and schizophrenia. Early screening and the integration of dual-diagnosis treatment strategies are essential to mitigate adverse outcomes in psychotic disorders.

Keywords: First-episode psychosis, drug-naïve, schizophrenia, substance use, clinical features

Öz

Amaç: Bu çalışmanın amacı, ilk atak psikoz (FEP) tanısı almış, ilaç-naif ve hastalığı yakın zamanda başlamış bireylerle şizofreni hastalarını madde ve sigara kullanımı açısından karşılaştırmak ve bu değişkenlerin sosyodemografik ve klinik özelliklerle ilişkisini incelemektir.

Yöntem: Çalışmaya 56'sı ilaç-naif FEP, 51'i ise şizofreni olgusu olmak üzere toplam 107 hasta dahil edilmiştir. Klinik değerlendirme için Klinik Genel İzlenim - Şiddet Ölçeği (CGI-S), Negatif Belirti Değerlendirme Ölçeği (SANS), Pozitif Belirti Değerlendirme Ölçeği (SAPS) ve Şizofrenide Depresyon için Calgary Ölçeği (CDSS) gibi standart ölçekler kullanılmıştır.

Bulgular: Madde kullanımı, şizofreni hastalarında (%41,2), FEP hastalarına (%25,0) göre daha yaygındı. Her iki grupta da madde kullanımı, artmış sigara ve alkol tüketimi ile birlikte daha yüksek klinik şiddet ile ilişkilidir. Özellikle, madde kullanan FEP hastalarında depresif ve negatif semptomlar anlamlı şekilde daha yüksektir ve hastalık şiddeti artmıştır. Şizofreni grubunda ise madde kullanımı, SAPS, SANS ve CGI-S skorlarının yüksekliği ile ve daha sık özkıyım davranışı ile ilişkilidir.

Sonuç: Madde kullanımı, hem FEP hem de şizofreni hastalarında semptom yükünü, davranışsal düzensizlikleri ve genel klinik şiddeti artırmaktadır. Psikotik bozukluklarda olumsuz sonuçları azaltmak için erken dönemde tarama yapılması ve ikili tanıya yönelik tedavi stratejilerinin entegrasyonu büyük önem taşımaktadır.

Anahtar kelimeler: İlk atak psikoz, ilaç kullanmamış, şizofreni, madde kullanımı, klinik özellikler

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Introduction

Psychosis is a severe psychiatric condition characterized by a loss of contact with reality, typically manifesting through hallucinations, delusions, and profound disturbances in thought, behavior, and affective regulation. A first episode of psychosis (FEP) refers to the initial manifestation of such symptoms and may occur at any point across the lifespan. The early phase, often described as "recent-onset," encompasses the initial years following symptom emergence and may evolve toward remission or progress into a chronic disorder such as schizophrenia (1,2).

The comorbidity between psychosis and substance use disorders (SUD) has emerged as a critical concern, given its markedly elevated prevalence in clinical populations compared to the general public. Epidemiological data consistently demonstrate disproportionately high rates of substance and tobacco use among individuals with both FEP and schizophrenia. In FEP samples, substance use has been reported in up to 42% of patients, with tobacco use ranging from 50% to 70% (3,4). These rates are even more pronounced among individuals with chronic schizophrenia, in whom substance use is observed in 47–60% of cases, and tobacco use reaches as high as 70–90% (5,6). In contrast, general population estimates range from 10–15% for substance use and 20–30% for tobacco use, underscoring a pronounced vulnerability among individuals with psychosis (7,8).

Cultural and geographical contexts further modulate the prevalence and patterns of substance use in schizophrenia. For instance, in the United States, approximately 47% of individuals with a lifetime diagnosis of schizophrenia or schizophreniform disorder meet the criteria for a co-occurring substance or alcohol use disorder (9). European studies report dual diagnosis prevalence rates ranging between 19% and 35%, highlighting significant cultural variability (5,10). Similarly, research from non-Western settings has revealed even higher rates. For example, an Indian study reported a 63.6% prevalence of SUD among schizophrenia patients, with nicotine being the most commonly used substance, followed by cannabis and alcohol (11). While methodological discrepancies across studies may partly account for these differences, environmental and sociocultural factors—such as drug accessibility, societal norms, and healthcare infrastructure—likely play a substantial role.

To account for this complex comorbidity, several explanatory models have been proposed. The diathesis-stress model suggests that substance use may act as an environmental catalyst that precipitates psychosis in biologically predisposed individuals (12). The self-medication hypothesis, in contrast, posits that substance use may serve as a coping mechanism to alleviate distressing psychiatric symptoms or to mitigate the side effects of antipsychotic treatment (13). A third framework proposes a shared neurobiological vulnerability—particularly dopaminergic dysregulation within the striatum—as a common etiological factor (14). Finally, the interactional model posits a reciprocal reinforcement between substance use and psychotic symptomatology, whereby chronic substance exposure or prolonged antipsychotic use may induce hypodopaminergic states, thereby exacerbating illness severity and promoting drug-seeking behavior (15).

The clinical consequences of substance use appear to vary significantly depending on the stage of illness. In individuals experiencing FEP, substance use is frequently associated with abrupt symptom onset, elevated positive symptoms, heightened paranoia, and increased agitation (16,17). In individuals with established schizophrenia, however, SUD is more commonly linked to exacerbated negative symptoms, poor adherence to treatment, increased relapse rates, and greater functional impairment (5). Additionally, comorbid SUD is associated with higher rates of self-harm, suicide attempts, and affective comorbidities. Notably, individuals with psychotic disorders already face a tenfold increased risk of suicide compared to the general population, and the presence of substance use amplifies this risk by an additional 30–50% (18–22). Emerging data also indicate that substance use may act as a precipitating factor in the onset of psychosis, particularly among vulnerable individuals (14,23,24). Moreover, tobacco use has been shown to alter the pharmacokinetics of antipsychotic medications via hepatic enzyme induction (e.g., cytochrome P450 1A2), thereby complicating pharmacological management (25).

These clinical challenges are especially pronounced in individuals with long-standing psychotic illnesses, in whom substance use patterns are often chronic and relapsing (26,27). In this subgroup, SUD has been identified as a robust predictor of adverse outcomes, including treatment disengagement, frequent rehospitalization, housing instability, aggression, involvement with the criminal justice system, and increased risk of medical comorbidities such as acquired immunodeficiency syndrome and hepatitis (27–30).

Given the substantial clinical, functional, and prognostic implications of comorbid substance use, a more refined understanding of its differential impact across the psychosis continuum remains critically important. Although prior literature has emphasized elevated substance use in schizophrenia, few studies have directly compared its prevalence, symptom correlates, and functional outcomes between drug-naïve individuals in the early stages of illness and those with chronic psychosis (31). To address this gap, the present study is guided by the hypothesis that substance use exerts stage-specific effects on clinical presentation, with variable influence on symptom domains and illness burden.

This study aims to empirically evaluate three key hypotheses: (1) Substance use is more prevalent among individuals with chronic schizophrenia compared to those experiencing a FEP, reflecting divergent illness trajectories and cumulative risk exposure. (2) Substance use is associated with greater symptom severity—including positive, negative, and depressive domains—as well as elevated global clinical burden in both groups. (3) The adverse clinical consequences of substance use are more pronounced in individuals with chronic schizophrenia, potentially due to neuroprogressive changes, behavioral sensitization, and cumulative psychosocial destabilization. Accordingly, this study seeks to determine the stage-specific clinical correlates of substance use in FEP and schizophrenia using standardized psychopathological assessments and comprehensive sociodemographic profiling.

Methods

Study Design and Setting

This cross-sectional, observational study was conducted at the Psychiatry Clinic of Ankara Gülhane Training and Research Hospital between February 1, 2022, and July 1, 2022. The study was carried out in a tertiary-level psychiatric hospital with a capacity of 120 inpatient beds and approximately 7,000 outpatient visits per month. This high-volume clinical setting, with its diverse psychiatric caseload, was particularly well-suited for observational studies examining the clinical characteristics of psychotic disorders. The study protocol was approved by the Gülhane Scientific Research Ethics Committee (Date: 06.01.2022, Decision No: 2022-15), and written informed consent was obtained from all participants in accordance with the ethical standards of the Declaration of Helsinki.

Sample

Participant recruitment and data collection were conducted at the outpatient follow-up unit for schizophrenia and other psychotic spectrum disorders at Gülhane Training and Research Hospital between February 1 and July 1, 2022. Patients were randomly selected from among follow-up and newly referred cases. A total of 182 cases were initially evaluated. Two experienced clinicians (ÖU, DFD) conducted all clinical assessments. Seventy-five patients were excluded due to refusal to provide informed consent (n = 54), unclear substance use history (n = 17), or acute substance-related conditions/substance-induced psychotic disorder (n = 4). The final sample consisted of 107 individuals aged 18 to 65 years and was divided into two subgroups. Schizophrenia group (n = 51): Patients with an established diagnosis who were receiving antipsychotic treatment. FEP group (n = 56): Drug-naïve individuals who had experienced their first psychotic episode within the previous six months and had not received prior psychiatric treatment. The operational definition of FEP was based on established criteria (32). All diagnoses were made by a board-certified psychiatrist (ÖU) according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (1).

Participants were eligible for inclusion if they were between 18 and 65 years of age and had a DSM-5 diagnosis of either schizophrenia or FEP. The schizophrenia group consisted of individuals currently receiving antipsychotic medication, while the FEP group comprised drug-naïve individuals within six months of their initial psychotic episode. All participants were required to provide written informed consent and demonstrate sufficient cooperation to undergo comprehensive clinical assessment. Exclusion criteria included psychosis secondary to general medical conditions or substance use, significant neurological or structural brain pathology, and uncooperative behavior that impeded reliable assessment (e.g., mutism or acute intoxication). Individuals suspected of having intellectual disability were also excluded. Although formal cognitive testing was not administered, clinical judgment was based on developmental history—particularly premorbid academic performance—and global functional capacity observed during psychiatric evaluation.

Measures

Sociodemographic and Clinical Data Form

A structured form developed by the research team was used to collect sociodemographic and clinical information, including age, sex, education level, marital and employment status, history of self-harming behavior, suicide attempts, and comorbid chronic medical conditions. Substance use was defined as the use of alcohol, illicit drugs, or prescription/nonprescription psychoactive substances that resulted in adverse clinical, functional, or social consequences within the 12 months prior to assessment. Substance use characteristics—including onset, duration, frequency, quantity, type, and methods of administration—were obtained through semi-structured clinical interviews. When available, collateral information from medical records, treating clinicians, and family members was used to enhance the accuracy of reporting.

Scale for the Assessment of Negative Symptoms (SANS)

Negative symptoms—such as affective flattening, alogia, avolition, and anhedonia—reflect deficits in emotional expressivity and goal-directed behavior. The SANS, developed by Andreasen (33), is a clinician-rated scale designed to assess the severity of negative symptoms in psychotic disorders. The Turkish version was validated by Erkoç et al. (34), with reported subscale Cronbach's alpha values as follows: affective flattening = 0.795, alogia = 0.758, apathy = 0.684, anhedonia = 0.754, attention deficit = 0.399, and total score = 0.914.

Scale for the Assessment of Positive Symptoms (SAPS)

Positive symptoms—including hallucinations, delusions, disorganized thinking, and bizarre behavior—represent the presence of abnormal mental functions. The SAPS is a 34-item clinician-rated scale developed by Andreasen (35) and is widely used to assess the severity of positive symptoms. The Turkish adaptation was validated by Erkoç et al. (36), with the following Cronbach's alpha coefficients: hallucinations = 0.772, delusions = 0.755, bizarre behavior = 0.610, formal thought disorder = 0.781, and total score = 0.844.

Calgary Depression Scale for Schizophrenia (CDSS)

The CDSS was specifically designed to differentiate depressive symptoms from negative and extrapyramidal symptoms in patients with schizophrenia (37). It consists of nine items rated during a semi-structured clinical interview. The Turkish version, validated by Oksay et al. (38), demonstrated excellent internal consistency (Cronbach's $\alpha = 0.90$).

Clinical Global Impression – Severity Scale (CGI-S)

The Clinical Global Impression – Severity scale is a widely used clinician-rated instrument that evaluates the overall severity of illness on a 7-point Likert scale. In the present study, only the CGI-S was utilized to capture a global impression of each participant's mental health status (39).

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics, version 22. Prior to data collection, a power

analysis was performed using G*Power software to determine the minimum sample size required to achieve adequate statistical power. Based on effect sizes reported in the literature, the required sample size was calculated as 86 participants (Group 1 = 43, Group 2 = 43), assuming an effect size of d = 0.72, power = 0.95, and α = 0.05. Descriptive statistics were computed for all variables. Continuous variables were presented as means and standard deviations, while categorical variables were reported as frequencies and percentages. The Kolmogorov–Smirnov test was used to assess the normality of distribution for continuous variables. For between-group comparisons: The Chi-square test or Fisher's exact test was applied for categorical variables, depending on expected cell frequencies. For continuous variables, independent samples t-tests were used when normality assumptions were met, while the Mann–Whitney U test was applied for non-normally distributed data. A p-value < 0.05 was considered statistically significant.

Results

Patients in the schizophrenia group were significantly older than those in the FEP group (mean age: 37.9 vs. 30.3 years; p = 0.003) and had lower levels of education and employment. No significant differences were observed between the groups regarding gender, marital status, place of residence, or living arrangement. The detailed sociodemographic and clinical characteristics of the sample are presented in Table 1.

Table 1. Demographic and clinical characteristics of the sample

Variable	FEP (n=56)	Schizophrenia (n=51)	Statistical analysis	P value
Age (years, mean ± SD)	30.36 ± 9.03	37.92 ± 13.18	Z=-3,013	0.003*
Education (years, mean ± SD)	12.34 ± 2.58	9.31 ± 3.53	Z=-4,452	0.000*
Gender (n; %)	Female: 15 (26.8%) Male: 41 (73.2%)	Female: 15 (29.4%) Male: 36 (70.6%)	df=1, χ2=0,091	0.763**
Marital status (n; %)	Single: 40 (71.4%) Married: 16 (28.6%)	Single: 39 (76.5%) Married: 12 (23.5%)	df=1, χ2=0,351	0.553**
Currently working (n; %)	27 (48.2%)	14 (27.5%)	df=1, χ2=4,869	0.027**
Place of residence (n; %)	Urban: 54 (96.4%) Rural: 2 (3.6%)	Urban: 47 (92.2%) Rural: 4 (7.8%)	Fisher's Exact=0,421	0.421**
Living arrangement (n; %)	With Family: 46 (82.1%) Alone: 10 (17.9%)	With Family: 46 (90.2%) Alone: 5 (9.8%)	df=1, χ2=1,436	0.231**
Smoking (n; %)	30 (53.5%)	36 (70.5%)	df=1, χ2=3,270	0.071**
Smoking amount (pcs/day, mean ± SD)	6.81 ± 10.62	18.67 ± 34.56	Z=-2,547	0.011*
Alcohol use (n; %)	18 (32.1%)	20 (39.2%)	df=1, χ2=0,583	0.445**
Substance use (n; %)	14 (25.0%)	21 (41.2%)	df=1, χ2=3,173	0.075**
Suicide attempt (n; %)	8 (14.3%)	15 (29.4%)	df=1, χ2=3,619	0.057**
Self-mutilation (n; %)	4 (7.1%)	18 (35.3%)	df=1, χ2=12,951	0.000**
CGI-Severity (mean ± SD)	5.00 ± 1.07	4.43 ± 1.23	Z=-2,451	0.014*
SANS Total (mean ± SD)	57.64 ± 15.36	57.50 ± 18.05	Z=-0,415	0.678*
SAPS Total (mean ± SD)	47.67 ± 13.10	44.21 ± 12.71	df=105; t=1,385	0.169***
CDSS Total (mean ± SD)	3.58 ± 2.14	3.13 ± 1.88	Z=-0,780	0.435*

*Mann-Whitney U Test, **Chi-Square Test, ***Student t-test; D: Standard Deviation, FEP: First-Episode Psychosis, CGI-Severity: Clinical Global Impression – Severity Scale, SANS: Scale for the Assessment of Negative Symptoms, SAPS: Scale for the Assessment of Positive Symptoms, CDSS: Calgary Depression Scale for Schizophrenia

Substance use was reported in 25.0% of individuals with FEP and in 41.2% of patients with schizophrenia. Although smoking rates were high in both groups, daily cigarette consumption was significantly higher in the schizophrenia group ($p = 0.011$). Self-mutilation behavior was also significantly more common among individuals with schizophrenia (35.3%) compared to those with FEP (7.1%) ($p < 0.001$). No statistically significant differences were found between the groups in terms of SANS, SAPS, and CDSS scores. However, CGI-Severity scores were significantly higher in the FEP group ($p = 0.014$), indicating more severe global clinical symptoms in this subgroup.

Table 2. Comparison of clinical characteristics according to substance use history in FEP patients

Variable	Substance Users (n=14)	Non-Substance (n=42)	Statistical analysis	p-value
Smoking (n; %)	12 (85.7%)	18 (42.8%)	df=1, χ^2=7,754	0.005*
Smoking amount (pcs/day, mean ± SD)	10.18 ± 10.59	5.69 ± 10.52	Z=-2,354	0.019**
Alcohol use (n; %)	8 (57.1%)	10 (23.8%)	Fisher's Exact=0,044	0.044***
Suicide attempt (n; %)	5 (35.7%)	3 (7.1%)	Fisher's Exact=0,018	0.018***
Self-mutilation (n; %)	3 (21.4%)	1 (2.4%)	Fisher's Exact=0,044	0.044***
CGI-Severity (mean ± SD)	6.07 ± 0.61	4.64 ± 0.95	Z=-4,428	0.000**
SANS Total (mean ± SD)	71.64 ± 13.58	52.97 ± 13.00	Z=-3,703	0.000**
SAPS Total (mean ± SD)	51.85 ± 16.12	46.28 ± 11.82	df=54, t=-1,390	0.170****
CDSS Total (mean ± SD)	4.78 ± 2.51	3.19 ± 1.87	Z=-2,086	0.037**

*Chi-Square Test, **Mann-Whitney U Test, ***Fisher's Exact Test, ****Student t-test*

Table 3. Comparison of clinical characteristics according to substance use history in schizophrenia patients

Variable	Substance Users (n=21)	Non-Substance (n=30)	Statistical analysis	p-value
Smoking (n; %)	19 (90.4%)	17 (56.6%)	df=1, χ^2=6,801	0.009**
Smoking amount (pcs/day, mean ± SD)	25.11 ± 37.16	14.16 ± 32.49	Z=-2,629	0.009*
Alcohol use (n; %)	18 (85.7%)	2 (6.7%)	df=1, χ^2=32,381	0.000**
Suicide attempt (n; %)	9 (42.9%)	6 (20.0%)	df=1, χ^2=3,109	0.078**
Self-mutilation (n; %)	12 (57.1%)	6 (20.0%)	df=1, χ^2=7,462	0.006**
CGI-Severity (mean ± SD)	5.38 ± 0.97	3.77 ± 0.93	Z=-4,602	0.000*
SANS Total (mean ± SD)	69.80 ± 19.32	48.90 ± 10.87	Z=-3,669	0.000*
SAPS Total (mean ± SD)	48.71 ± 14.45	41.06 ± 10.46	df=49, t=-2,194	0.033***
CDSS Total (mean ± SD)	3.28 ± 2.07	3.03 ± 1.77	Z=-0,273	0.785*

*Statistical Tests: *Mann-Whitney U, **Chi-Square, ****Student t-test*

Within the FEP group, individuals with a history of substance use exhibited significantly higher rates of smoking ($p = 0.005$), alcohol consumption ($p = 0.044$), suicide attempts ($p = 0.018$), and self-harm ($p = 0.044$) compared to their non-using counterparts. These patients also had significantly elevated scores on the CGI-S ($p < 0.001$), SANS ($p < 0.001$), and CDSS ($p = 0.037$) scales, reflecting greater overall symptom

severity and depressive burden. Among patients with schizophrenia, those with a history of substance use demonstrated significantly higher levels of smoking ($p = 0.009$), alcohol use ($p < 0.001$), and self-mutilation behavior ($p = 0.006$). Furthermore, they had significantly elevated CGI-S ($p < 0.001$), SANS ($p < 0.001$), and SAPS ($p = 0.033$) scores compared to non-users, indicating greater symptom severity. However, there were no significant differences in CDSS scores.

In the direct comparison of substance-using patients across the two diagnostic groups, self-mutilation behavior was significantly more prevalent in the schizophrenia group ($p = 0.036$). Conversely, CGI-S scores were significantly higher in the FEP group ($p = 0.033$), suggesting a greater overall clinical burden among substance-using individuals with recent-onset psychosis.

Discussion

This study aimed to investigate the differential impact of substance use in individuals with FEP and schizophrenia. Although substance use was numerically more frequent among schizophrenia patients (41.2%) than FEP patients (25.0%), this difference did not reach statistical significance ($p = 0.075$). Therefore, the hypothesis that substance use is significantly more prevalent in chronic psychosis than in early-stage psychosis was not empirically supported. Despite the lack of statistical significance, the observed prevalence rates are clinically meaningful and consistent with a broader body of literature reporting substance use rates between 30% and 50% in psychotic disorders (40–43). Both rates identified in the present study substantially exceed the estimated 16% prevalence in the general population, underscoring the disproportionate burden of comorbid substance use in this clinical population (44).

Substance use was also associated with more severe clinical profiles across both diagnostic groups. Specifically, individuals with comorbid substance use exhibited greater overall illness severity, increased rates of cigarette and alcohol consumption, and poorer functional outcomes. These associations support the conceptualization of substance use as an exacerbating factor that amplifies the clinical burden of psychosis.

When contextualized within national data from Türkiye, the present findings reveal a striking increase in substance use prevalence among individuals with psychotic disorders. Historical estimates reported prevalence as low as 5.2% among schizophrenia patients in 2003 (45). A 2004 study found smoking rates as high as 69.4%, but cannabis use remained relatively rare at 2.2% (46). Furthermore, a 2008 study focusing on FEP patients reported a substance use prevalence of just 10.8% (47). In contrast, the markedly higher prevalence rates observed in the current study may reflect shifting sociocultural dynamics, increased accessibility to psychoactive substances, and evolving patterns of psychiatric comorbidity over the past two decades. These findings underscore the necessity of reevaluating substance use as a significant and potentially escalating component of psychosis, particularly in the context of changing national and cultural landscapes.

Subgroup analyses based on substance use history revealed notable clinical distinctions within both diagnostic groups. Among patients with FEP, those who reported substance use demonstrated significantly higher rates of cigarette smoking, alcohol consumption, suicide attempts, and self-injurious behaviors compared to non-using counterparts. These findings suggest that, even during the early stages of psychotic illness, substance use may act as a catalyst for affective instability and behavioral dysregulation, thereby complicating both clinical presentation and long-term prognosis.

The relationship between substance use and self-injurious behavior in individuals with psychotic disorders appears to be inherently bidirectional. A notable finding of the study was the significantly higher prevalence of self-mutilation among schizophrenia patients (35.3%) compared to FEP patients (7.1%). Substance use further increased the likelihood of self-injurious behavior in both groups, with the highest rates observed among substance-using schizophrenia patients (57.1%). While the cross-sectional design prevents causal inference, these results support prior literature suggesting a bidirectional relationship between substance use and behavioral dysregulation in psychosis (26,31,48).

The findings also emphasize the importance of considering suicidality. In the FEP group, substance users had significantly higher rates of suicide attempts compared to non-users (35.7% vs. 7.1%, p = 0.018), whereas in schizophrenia, the association did not reach statistical significance (p = 0.078). These differences may reflect developmental, neurobiological, or psychosocial factors that render early-stage patients more vulnerable to impulsivity and affective instability under the influence of substances (48-50). These findings are consistent with previous literature indicating that substance use substantially contributes to the risk of self-directed violence and suicide among individuals with psychotic disorders (51–53).

Nevertheless, emerging evidence suggests that early and targeted intervention can mitigate the course of comorbid substance use. Longitudinal studies have shown that integrated early intervention programs are associated with a reduction in substance use disorders among FEP patients. For example, Abdel-Baki et al. (54) reported a significant decline in SUD prevalence over a two-year follow-up period among FEP patients who received comprehensive, phase-specific treatment. These findings highlight the critical importance of initiating timely and integrated interventions in the early stages of psychotic illness, which may not only enhance short-term clinical outcomes but also reduce the risk of long-term behavioral complications and illness progression.

Importantly, substance use was significantly associated with increased clinical severity across both diagnostic groups. In the FEP subgroup, substance users exhibited significantly higher scores on CGI-S, SANS, and CDSS scales compared to non-users, reflecting a heightened burden of negative and depressive symptoms. In contrast, substance-using schizophrenia patients had elevated scores on SAPS, SANS, and CGI-S, indicating an association between substance use and both positive and negative symptomatology in chronic psychosis. However, depressive symptom severity did not differ significantly in schizophrenia patients based on substance use status, suggesting that depressive symptoms may be more sensitive to substance use during early illness stages. These findings suggest that substance use may exert stage-specific effects on symptom dimensions (55). In FEP patients, depressive and negative symptoms appear particularly susceptible, whereas in chronic schizophrenia, substance use is more closely linked to the exacerbation of positive symptoms. This distinction may be explained by differences in neurobiological sensitivity and illness progression across stages.

From a neurobiological perspective, substance use may exacerbate negative symptoms—such as avolition, emotional withdrawal, and anhedonia—through its disruptive effects on mesolimbic dopaminergic reward circuitry (56). Chronic exposure to psychoactive substances may further diminish motivation and affective responsivity, thereby amplifying pre-existing deficits in goal-directed behavior. In FEP patients, depressive symptoms appear particularly sensitive to the destabilizing effects of substance use, possibly due to early neuroadaptive changes and compounded psychosocial stressors associated with dual diagnosis status (57).

With regard to positive symptoms, the elevated SAPS scores observed in schizophrenia patients with a history of substance use may reflect a sensitization process. Repeated exposure to psychoactive substances—particularly cannabis and stimulants—may lower the threshold for psychotic experiences, consistent with evidence indicating that substance use alters dopaminergic transmission in a way that increases susceptibility to hallucinations and delusions (58).

These symptom-specific associations are further supported by explanatory models such as the self-medication hypothesis, which posits that individuals may engage in substance use to relieve distressing psychotic symptoms or to mitigate the side effects of antipsychotic medications (13). The shared vulnerability hypothesis provides a complementary framework, proposing that converging genetic, neurobiological, and environmental risk factors predispose individuals to both psychotic disorders and substance use disorders (14). These overlapping vulnerabilities may contribute to a clinical phenotype characterized by increased symptom severity, treatment resistance, and greater functional impairment.

Although direct measures of functional status were not included, the significantly higher CGI-S scores in both substance-using subgroups suggest an overall greater illness burden. This global increase in clinical severity aligns with the stepwise progression model proposed by Eiden et al. (59), which posits that

substance use functions as a compounding factor—exacerbating symptom severity, impairing psychosocial functioning, diminishing adherence to pharmacological and psychosocial interventions, and ultimately contributing to poorer long-term clinical and functional outcomes (52,60,61).

Taken together, these findings reinforce the conceptualization of substance use not as a coincidental or secondary comorbidity, but rather as a central, dynamic, and clinically consequential component of psychotic illness. Substance use exerts measurable influence across multiple domains, including symptom expression, behavioral risk (e.g., suicidality, self-injury), and treatment responsiveness. Its presence complicates illness trajectories, restricts recovery potential, and heightens the risk of enduring disability (62).

This study has several limitations that should be considered when interpreting its findings. First, the cross-sectional design prevents causal inferences regarding the directionality between substance use and clinical severity. Consequently, it remains unclear whether substance use exacerbates symptomatology or whether individuals with more severe psychopathology are more likely to engage in substance use. Second, the study was conducted at a single clinical center, which may limit the generalizability of the results to broader, community-based, or more heterogeneous populations. Third, data on substance use were collected through self-report, raising potential concerns about recall and social desirability biases—particularly in contexts where stigma surrounding substance use remains prominent. Fourth, the relatively small sample sizes in subgroup analyses may have limited the statistical power to detect subtle or interactional effects. Fifth, the study did not differentiate between specific types of substances, thereby restricting conclusions regarding substance-specific impacts (e.g., cannabis vs. stimulants vs. alcohol). Finally, while individuals suspected of having intellectual disabilities were excluded, no formal cognitive assessments were administered. Instead, exclusions were based on clinical judgment informed by developmental history, academic performance, and functional observations, which may have resulted in misclassification or underrecognition of cognitive impairments.

In conclusion, this study demonstrates that comorbid substance use in psychotic disorders is associated with increased clinical severity, affective and behavioral dysregulation, and elevated risk for self-harm, regardless of illness stage. Although the prevalence of substance use was higher in patients with schizophrenia, this difference was not statistically significant. Instead, substance use appears to exert symptom-specific and stage-sensitive effects—most notably intensifying depressive symptoms in FEP and positive symptoms in chronic schizophrenia. Given these findings, substance use should not be viewed as a peripheral or secondary concern in psychotic disorders, but rather as a central clinical factor warranting routine assessment and intervention. Clinical services should prioritize integrated dual-diagnosis treatment models, especially in the early stages of illness where the potential for long-term stabilization is greatest.

Future research should employ longitudinal designs to clarify causal relationships, include functional and treatment adherence measures, and explore substance-specific effects on clinical outcomes. Such efforts will contribute to the development of tailored, evidence-based strategies aimed at reducing the substantial burden imposed by comorbid substance use in psychotic populations.

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Yazar Katkıları: Tüm yazarlar ICMJE'in bir yazarda bulunmasını önerdiği tüm ölçütleri karşılamışlardır
Etik Onay: Bu çalışma için ilgili Etik Kuruldan etik onay alınmıştır.
Hakem Değerlendirmesi: Dış bağımsız.
Çıkar Çatışması: Yazarlar çıkar çatışması olmadığını beyan etmişlerdir.
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Not: Bu çalışma ilk yazarın ikinci yazarın danışmanlığında yürüttüğü tez çalışmasından üretilmiştir.

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