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Factors Associated with Psychotic and Depressive Symptoms in Methamphetamine Users

Sercan Karabulut[1*]

Abstract

Objective: Methamphetamine use has been recognized as a prominent public health issue, which is associated with psychotic and depressive symptoms. This study aimed to assess factors that show a significant relation with psychotic and depressive symptoms in adults who use methamphetamine.
Method: We assessed 95 patients who had used methamphetamine within the last month and were admitted to the outpatient treatment clinic. Evaluation of all patients was carried out through face-to-face interviews, and their symptoms were evaluated using different scales. The Scale for the Assessment of Positive Symptoms and the Scale for the Assessment of Negative Symptoms were employed to assess positive and negative symptoms of psychosis, respectively. Depressive symptoms were measured using the Montgomery-Asberg Depression Rating Scale, while illness severity was evaluated using the Clinical Global Impression- Severity Scale. Additionally, functioning status was assessed using the Functioning Assessment Short Test, and withdrawal severity was measured by employing the Amphetamine Cessation Symptom Assessment Scale. Craving severity was evaluated using the Stimulant Craving Questionnaire, anxiety severity using the Hamilton Anxiety Rating Scale, and insight status using the Schedule for Assessment of Insight Expanded.
Results: Among the demographic variables, working with family was associated with lower positive symptoms scores (OR = 6.31, P < 0.05). Parole/probation related admissions were associated with lower positive and depressive symptoms scores (OR = 15.06, P = 0.03; OR = 9.87, P = 0.02). Having suicide attempts, number of suicide attempts, and amount of methamphetamine used were found to show association with higher positive (OR = 13.59, P < 0.01; OR = 2.52, P < 0.05; OR = 3.48, P < 0.05, respectively) and depressive symptoms scores (OR = 10.35, P < 0.001; OR = 2.23, P < 0.01; OR = 2.3, P < 0.05). After adjusting for all variables, clinical impression and insight scores remained significantly associated with positive symptoms scores (AOR = 6.74, P < 0.05; AOR = 2.63, P < 0.001, respectively), while anxiety, amphetamine cessation, and positive symptoms scores remained associated with depressive symptoms scores (AOR = 0.48, P < 0.001; AOR = 0.11, P = 0.003; AOR = 0.36, P = 0.02, respectively).
Conclusion: This study appears to be the first to examine the associations between clinical variables and both positive symptoms and depressive symptoms in methamphetamine users. Increased attention should be paid to suicide history, anxiety level, amount of methamphetamine use and loss of insight to provide effective treatment in patients with methamphetamine use.

Key words: *Depression; Methamphetamine; Psychosis; Substance Use*

1. Centre of Alcohol and Substance Addiction Treatment, Ataturk State Hospital, Antalya, Turkey.

***Corresponding Author:**
Address: Nebiler Mahallesi, 7192 Sokak, Kepez/Antalya, Turkey Postal Code: 07192.
Tel: 90-5356127720, Fax: 90-2423454550, Email: drs_karabulut@hotmail.com

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Methamphetamine is an illicit substance with psychostimulant effects on users that have been reported all over the world since 1950s (1). It is estimated that there exist approximately 27 million substance users of amphetamine-type stimulants (2). As all psychostimulants, methamphetamine may cause serious physical and mental problems; especially psychosis occurs more often in regular users, exceeding 50 % in some reports (3-6). Methamphetamine may also lead to reduction of sleep duration and appetite, changes in mood as well as social and sexual functions (7). The prevalence of methamphetamine use disorder has been reported to increase in both Europe and Asia since the last decade (8, 9).

Growing evidence suggests that stimulant drugs such as methamphetamine may evoke psychotic symptoms in patients with primary psychotic disorders. Moreover, drug use may even produce psychotic symptoms in individuals without any history of premorbid illnesses (10-12). It has been well-known that individuals with methamphetamine-related psychosis show more severe clinical symptoms, more serious emergency service admissions, and worse illness courses than patients without psychosis. Studies have shown that 26% to 46% of methamphetamine users have methamphetamine-related subclinical or clinical psychotic symptoms (8). Studies conducted on individuals who use methamphetamine and experience psychotic symptoms have indicated that these patients can be roughly divided into two groups. One group includes patients who suffer from transient psychotic symptoms that disappear shortly after stopping methamphetamine use, while the other group consists of patients who suffer long-term psychotic symptoms which persist during weeks or months of abstinence (13). In a recent study, transient psychotic symptoms included paranoid delusions and tactile hallucinations, while persistent psychotic symptoms were characterized by delusions of reference, thought reference, and auditory hallucinations (14). In various studies, the time between the first methamphetamine use and the appearance of psychotic symptoms was reported in a wide range of 1.7 to 5.2 years (15). In a cross-sectional study, it was found that the age at first drug use, amount of drug use, schizoid, schizotypal and antisocial personality traits scale scores, major depressive disorder, and alcohol use disorder were related with psychosis (10).

Epidemiological data indicate that % 41.6 of stimulant users have a lifetime history of depression (16). Studies assessing depressive symptoms in methamphetamine users have shown a significant increase in depression and related suicide attempt rates, even though depressive symptoms may also be seen in the withdrawal stage (17). Recently, an affective component including elevated levels of depression and anxiety as a dimension of exacerbated symptoms related to methamphetamine use has been discovered (11). These symptoms make it difficult to distinguish clusters of psychiatric symptoms and cross-sectional diagnostic evaluation in methamphetamine users. Thus, it seems difficult to decide which symptoms arise from primary mood and/or psychotic disorder or a substance use disorder, which can be challenging for clinicians when deciding treatment plans (18, 19). Excluding patients with major psychiatric disorders in clinical trials may not offer a definitive solution due to the presence of subclinical symptoms.

Studies investigating symptom clusters in methamphetamine users have demonstrated that a subgroup of patients reported significant anxiety and depressive symptoms without severe psychotic symptoms. Moreover, symptoms such as irritability, disorganized thought contents, and psychomotor hyperactivity were more frequent in those with more severe psychosis (20).

Recent studies have examined the negative symptoms in methamphetamine users distinct from the diagnosis of schizophrenia. Results in these studies suggest that although there was a subgroup with negative symptoms, methamphetamine-related depression and/or methamphetamine-associated psychosis were not occurring within the same syndrome (21).

In this perspective, analyzing the affective and psychotic subgroups with their unique features and identifying the factors related to these symptoms have become essential to shed light on the dynamics of methamphetamine use disorder. In the light of the above-mentioned evidence, this study was planned to investigate the risk factors for psychosis and depression in patients who use methamphetamine. While studies assessing factors related to methamphetamine-associated psychosis have reported limited data about concomitant symptoms, in this study we planned to investigate all clinical factors and their relations with psychotic and depressive symptoms discretely. Furthermore, in this research we examined the substance-related correlates of psychotic and depressive symptoms including methamphetamine use pattern and intensity. To differentiate confounding factors, patients with psychiatric disorders and regular use of other substances, except for tobacco products, were excluded from the study. In Turkey, to our knowledge, there is no study which has investigated methamphetamine use and related symptoms.

Materials and Methods

Procedure of the Study

The present study was administered at the Ataturk State Hospital Outpatient Alcohol and Drug Addiction Treatment Clinic (OTC) in Antalya, Turkey, between September 2020 and February 2022. This study was planned as a prospective study, with patients being followed up to six months after their treatment entry.

To avoid confounding factors, we deliberately determined the eligibility criteria to be relatively restrictive. All patients were screened with a structured

interview (SCID-5-CV) for stimulant (methamphetamine) use disorder (22, 23). Male and female participants aged 18 years or above with the diagnosis of methamphetamine use disorder were included in the study. Other inclusion criteria were as follows: applying to the OTC for substance use disorder treatment, giving informed consent, completing forms thoroughly, and providing a urine sample. In addition, knowing the Turkish and English languages at least at a sufficient level was necessary for participation in the study. After study inclusion, the participants were examined to determine the duration since their last methamphetamine use. Those who had not used the drug in the last 30 days were excluded from the study. Furthermore, those who had used any substance without methamphetamine within the last 180 days before the study participation, had medical conditions with clinically significant impairment or undergone psychiatric treatment in residential or outpatient clinic within the last 180 days prior to the study participation, met the substance or alcohol use disorder criteria (based on the DSM-5) except methamphetamine and nicotine, had any legal problems that could preclude consistent participation, were excluded from the study. All patients were screened with urine toxicology tests, and any patient testing positive for substances other than methamphetamine was excluded from the study.

The minimum value of the sample required for the study was calculated using the G-Power program. The sample population calculations indicated that a minimum of 34 participants with a probability of 95 %, an error margin of 5 %, and an effect size of 80 % were required.

A total of 95 patients who had consecutively admitted to the OTC met the study criteria and were recruited into this research. Evaluation of all patients was carried out through face-to-face interviews. These patients were repeatedly evaluated at admission and over the subsequent six months. For the current publication, we used data collected during the initial evaluation period. The Antalya Training and Research Hospital Ethics Committee reviewed and approved our study (approval number: 5/19). Furthermore, all subjects were contacted and informed by the author. The research adhered to the ethical terms of the World Medical Association Declaration.

Measures

Methamphetamine Use

Methamphetamine use measurements included various parameters, including the amount of use within the last month, the frequency of use within the last month (daily, two to six times a week, weekly or less than once a week), the main route of administration, the age at the first methamphetamine use, and the duration of frequent or problematic methamphetamine abuse. Urine toxicology screening was used for every admission.

Demographics

Demographic measurements included age, sex, insurance, income, employment, schooling and marital status, frequency and amount of tobacco and alcohol use, screening for infectious diseases (HBV, HCV, HIV, VDRL-TPHA) and history of suicide attempts.

Clinical Scales

In our study, we used the Scale for the Assessment of Positive Symptoms (SAPS) to determine positive symptoms and their severity (24). During the scale evaluation, the information obtained from the relatives of the patient was also taken into account in addition to the observations about the patient. A high score obtained from the scale shows the high severity of the patient's positive symptoms. The analysis of the Turkish validity and reliability of the scale was performed by Erkoc *et al*. (25).

The Scale for the Assessment of Negative Symptoms (SANS) was employed to measure the level of negative symptoms in schizophrenia. During the scale evaluation, the information obtained from the relatives of the patient was also considered in addition to the observations about the patient. The SANS consists of 19 negative symptom items; these items were also clustered into five global factor ratings (26). The SANS total score was determined by summing up all these ratings. The analysis of the Turkish validity and reliability of the scale was performed by Erkoc *et al.* (27).

The Montgomery-Asberg Depression Rating Scale (MADRS) evaluates both cognitive and somatic symptom clusters while determining the severity of depressive symptoms. As each item is scored from 0 to 6, the 10 item-scale is rated for a total possible maximum score of 60. While making the evaluation, the practitioner takes into account the symptoms observed in the last seven days. A high score of this scale indicates the high severity of depressive symptoms (28). The analysis of the Turkish validity and reliability of the scale was performed by Suzan *et al.* (29).

The Clinical Global Impression-Severity Scale (CGI-S) is a clinician-administered scale used to rate the severity of illness from 1 to 7 (30).

The Functioning Assessment Short Test (FAST) was used to assess the individual's capacity to perform daily activities and social functionality. The FAST is a clinician-rated brief instrument designed to evaluate the main functioning impairments. The scale contains 24 items which assess impairment in six areas of functioning: autonomy, occupational functioning, cognitive functioning, financial issues, interpersonal relationships, and leisure time (31). The analysis of the Turkish validity and reliability of the scale was performed by Aydemir *et al.* (32).

The Amphetamine Cessation Symptom Assessment Scale (ACSA) was used to assess withdrawal severity. The ACSA is an observer-rated scale with 16 items for assessing the severity of amphetamine withdrawal symptoms. Each question is scored from 0 to 4. A total score is calculated by summing all those items for a total possible maximum score of 64. When the scale score is high, it indicates the high severity of withdrawal

symptoms (33). The Stimulant Craving Questionnaire (STCQ) was used to measure craving severity. The 10-item STCQ is a clinician rating tool to assess stimulant craving. Participants were requested to indicate their feelings on a 0 to 6 scale (34). By summing those 10 items, the total scale score is obtained. The Hamilton Anxiety Rating Scale (HAM-A), which was developed as a clinician-rated, was selected to quantify symptoms of anxiety in this study. The commonly used 14-item version was conducted in the current study, with higher scores related to greater anxiety symptom severity (35). The Turkish validity and reliability study of HAM-A was reported by Yazıcı *et al*. (36). In order to evaluate three different dimensions of insight separately, the Schedule for Assessment of Insight Expanded (SAI-E) scale was preferred in this study. The commonly used eight-item version of this scale was conducted in the current study. Aslan *et al*. published the validity and reliability study of the SAI-E in Turkish (37, 38).

Statistical Analyses

Descriptive statistics were used to analyze numerical data, presented as mean ± standard deviation, and categorical variables, presented as frequency and percentages. To examine the factors related to depressive and psychotic symptoms, a two-stage analysis was performed. In the first stage, based on the literature, all potential useful clinical and sociodemographic values were separately compared in terms of MADRS scores (a total score of 19 or lower vs. a total score of 20 or greater) and SAPS scores (≥ 3 scores on any of the items of hallucinations or delusions as clinically significant vs nonsignificant). The chi-square test was used to analyze nominal values, while the independent t-test was employed to examine numerical values. In the second stage, linear regression analyses were performed using SAPS and MADRS as predictors. Based on the analysis results, unadjusted and adjusted odd ratios (OR) were calculated. In the adjusted models, significant variables which were found out in the first stage were included. The Durbin-Watson test was applied, and its d value between 1 and 3 indicates that the model has no first-order autocorrelation. The level of significance was set at 0.05.

Results

Sample Characteristics

According to the calculations, the mean age of the sample was 29.4 ± 6.6 years. The majority of the participants were male (80%), and almost four-fifths (83.2%) were living with their families. About 46.3% of them were unemployed, and 45.3% were single. 51.6% had admitted to clinic voluntarily (Table 1).

Table 1. Sociodemographic Characteristics of Patients with Methamphetamine Use

Gender	**n**	**%**	**Lives with**	**n**	**%**
Male	76	80	Family	79	83.2
Female	19	20	Alone	10	10.5
Income Status			Friend/shelter/homeless	6	6.3
None	41	43.2	**Insurance**		
Low income (0-4250 TL)	12	12.6	Yes	56	58.9
Middle income (4250-15000 TL)	28	29.5	No	39	41.1
High income (> 15000 TL)	14	14.7	**Schooling**		
Working Status			Primary school (5 years)	17	17.9
Unemployed	44	46.3	Secondary school (8 years)	49	51.6
Temporary employee	10	10.5	High school (12 years)	25	26.3
Regular employee	38	40	University	4	4.2
Works with family	3	3.2	**Admission**		
Marital Status			Voluntarily	49	51.6
Single	43	45.3	By family request	28	29.5
Married/In a relationship	33	34.7	Social services	3	3.2
Divorced	19	20	Probation	15	15.7
Tobacco Use			**Frequency of MA Use**		
Yes	92	96.8	Daily	47	49.5
None	3	3.2	More than weekly	27	28.4
Contagious Diseases			Less than weekly	21	22.1
Anti-HIV positive	-	-	**Route of Administration**		

HBV screening positive	1	1.1	Smoking	87	91.6
Syphilis screening positive	2	2.1	Injection	4	4.2
HCV screening positive	3	3.2	Oral	2	2.1
Suicide Attempt			Intranasal	2	2.1
Yes	36	37.9	**Urine Toxicology for MA**		
None	59	62.1	Positive	69	72.6
			Negative	26	27.4

	n	Mean	SD
Age (years)	95	29.4	6.6
Amount of cigarettes smoked (pack/year)	95	12	10.7
Amount of methamphetamine used (gr)	86	1	1.4
Age of first use of methamphetamine (years)	95	26.4	6.5
Duration of iv methamphetamine use (month)	95	0.3	2.5
Duration of methamphetamine use (month)	95	24	19.4
Number of suicide attempts	95	1	1.8
MADRS total score	92	24.1	13
HARS total score	92	19.8	10.7
CGI score	92	4.6	1.2
SAPS total score	92	25.2	20.7
SANS total score	92	23.5	14.9
SAI-E total score	92	10.3	3.5
ACSA total score	92	28.7	13.2
STCQ total score	92	20.7	16.2
FAST total score	92	39.3	17.4

TL: Turkish Liras, MA: Methamphetamine, SD = Standard Deviation, MADRS = Montgomery Asberg Depression Rating Scale, HARS = Hamilton Anxiety Rating Scale, CGI = Clinical Global Impression, SAPS = Scale for the Assessment of Positive Symptoms, SANS = Scale for the Assessment of Negative Symptoms, FAST = Functioning Assessment Short Test, SAI-E = Schedule for Assessment of Insight Expanded, ACSA = Amphetamine Cessation Symptom Assessment Scale, STCQ = Stimulant Craving Questionnaire.

Methamphetamine Use

Participants reported frequent use of methamphetamine, with a mean duration of 24 ± 19.4 months. The mean age at the first methamphetamine use was 26.4 years. Smoking was the most common route of administration (91.6%), with 49.5% reporting daily methamphetamine use and 28.4% using this substance more than once a week (28.4%). At the time of admission, the majority of participants had positive urine toxicology results for methamphetamine (62.1%).

Relationship of Socio-Demographic and Clinical Variables to SAPS Scores

Among demographic variables, working with family (as a family business, generally supervised by parents or siblings) was associated with lower SAPS scores (OR = -6.31, 95% CI [-30.56, 17.93]). But significance disappeared after adjusting for all variables. Furthermore, probation/parole associated admissions were associated with lower SAPS scores (OR = -15.06, 95% CI [-27.18, -2.94]) Similar to previous findings, association failed to achieve significance after adjustment. Having suicide attempts and number of suicide attempts showed a significant association with higher SAPS scores (OR = 13.59, 95% CI [5.16, 22.01]; OR = 2.52, 95% CI [0.26, 4.78], respectively), even though significance vanished after adjustment. The amount of methamphetamine used was found to be associated with higher SAPS scores (OR = 3.48, 95% CI [0.29, 6.68]). Among clinical scales, all MADRS, HARS, CGI, SANS, ACSA and FAST scores were positively associated with SAPS scores; however, SAI-E scores were negatively associated with SAPS scores. After adjusting for all variables, CGI and SAI-E scores remained significantly associated (OR = 6.74, 95% CI

[1.62, 11.86]; OR = -2.63, 95% CI [-3.71, -1.54], respectively) (Table 2).

Relationship of Socio-Demographic and Clinical Variables to MADRS Scores

Parole/probation associated admissions were associated with lower MADRS scores, although significance disappeared after adjusting for all variables (OR = -9.87, 95% CI [-17.47, -2.28]). Having suicide attempts and number of suicide attempts were positively associated and both positive associations changed after adjustment (OR = 10.35, 95% CI [5.2, 15.5]; OR = 2.23, 95% CI [0.85, 3.61], respectively). The amount of methamphetamine used was associated with higher MADRS scores (OR = 2.3, 95% CI [0.34, 4.26]). Among clinical scales, all SAPS, HARS, CGI, SANS, ACSA, SCTQ and FAST scores were positively associated with MADRS scores. After adjusting for all variables, HARS and ACSA scores remained positively associated; however, SAPS scores were negatively associated (OR = 0.48, 95% CI [0.24, 0.72]; OR = 0.36, 95% CI [0.12, 0.6], OR = - 0.11, 95% CI [-0.2, -0.02], respectively) (Table 3).

Table 2. Factors Associated with Scale for the Assessment of Positive Symptoms Score (Linear Regression Results)

SAPS	OR (95 % CI)	Adjusted OR (95 % CI)
Current job status		
Unemployed	1	1
Temporary employee	0.23 (-14.64 – 15.12)	2.45 (-10.87 – 15.7)
Regular employee	-10.38 (-19.48 - -1.27)	-2.54 (-10.97 – 5.87)
Works with family	-6.31 (-30.56 – 17.93)*	-4.22 (-22.76 – 14.3)
Admission		
Voluntarily	1	1
By family request	4.83 (-4.67 – 14.33)	2.47 (-5.89 – 10.84)
Social services	-4.94 (-28.64 – 18.75)	-1.13 (-20.11 – 17.84)
Probation	-15.06 (-27.18 – -2.94)*	-3.84 (-14.41 – 6.71)
Suicide Attempt		
No	1	1
Yes	13.59 (5.16 – 22.01)**	3.2 (-7.91 – 14.33)
Number of suicide attempts	2.52 (0.26 – 4.78)*	0.57 (-2.08 – 3.23)
Amount of methamphetamine used (gr)	3.48 (0.29 – 6.68)*	-0.08 (-2.62 – 2.46)
MADRS score	0.57 (0.26 – 0.88)***	-0.4 (-0.92 – 0.1)
HARS score	0.84 (0.48 – 1.2)***	0.38 (-0.18 – 0.95)
CGI score	10.01 (7.3 – 12.73)***	6.74 (1.62 – 11.86)*
SANS score	0.52 (0.25 – 0.78)***	0.08 (-0.28 – 0.46)
SAI-E score	-3.23 (-4.24 – -2.23)***	-2.63 (-3.71 – -1.54)***
ACSA score	0.8 (0.52 – 1.08)***	0.16 (-0.36 – 0.69)
FAST score	0.57 (0.35 – 0.79)***	-0.09 (-0.42 – 0.23)

OR(CI): Odds Ratio (confidence interval), MA: Methamphetamine, MADRS = Montgomery Asberg Depression Rating Scale, HARS = Hamilton Anxiety Rating Scale, CGI = Clinical Global Impression, SANS = Scale for the Assessment of Negative Symptoms, FAST = Functioning Assessment Short Test, SAI-E = Schedule for Assessment of Insight Expanded, ACSA = Amphetamine Cessation Symptom Assessment Scale.
*P-value < 0.05,**P-value < 0.01, ***P-value < 0.001.

Table 3. Factors Associated with Montgomery Asberg Depression Rating Scale Score (Linear Regression Results)

MADRS	OR (95 % CI)	Adjusted OR (95 % CI)
Admission		
Voluntarily	1	1
By family request	-5.2 (-11.15 – 0.75)	-1.69 (-5.39 – 2.01)
Social services	7.64 (-7.2 – 22.49)	1.49 (-7.3 – 10.28)
Probation	- 9.87 (-17.47 - - 2.28)*	- 1.1 (-5.93 – 3.73)
Alcohol use		
None	1	1
Social use	3.38 (-0.84 – 7.62)	2.02 (- 0.65 – 4.69)
Suicide Attempt		
No	1	1
Yes	10.35 (5.2 – 15.5)***	0.65 (-4.44 – 5.75)
Number of suicide attempts	2.23 (0.85 – 3.61)**	0.71 (-0.54 – 1.97)
Amount of methamphetamine used (gr)	2.3 (0.34 – 4.26)*	0.09 (-1.12 – 1.3)
Age of first methamphetamine use (years)	- 0.39 (- 0.79 – 0.01)	0.13 (- 0.11 – 0.38)
HARS score	0.97 (0.82- 1.12)***	0.48 (0.24 – 0.72)***
SAPS score	0.22 (0.1 – 0.34)***	- 0.11 (-0.2 – - 0.02)*
CGI score	6.61 (4.96 – 8.26)***	0.98 (-1.52 – 3.48)
SANS score	0.3 (0.13 – 0.47)**	0.05 (-0.12 – 0.22)
ACSA score	0.78 (0.65 – 0.9)***	0.36 (0.12 – 0.6)**
STCQ score	0.36 (0.21 – 0.51)***	- 0.03 (-0.15 – 0.07)
FAST score	0.45 (0.33 – 0.58)***	0.11 (-0.32 – 0.26)

OR (CI): Odds Ratio (confidence interval), MA: Methamphetamine, HARS = Hamilton Anxiety Rating Scale, CGI = Clinical Global Impression, SAPS = Scale for the Assessment of Positive Symptoms, SANS = Scale for the Assessment of Negative Symptoms, FAST = Functioning Assessment Short Test, ACSA = Amphetamine Cessation Symptom Assessment Scale, STCQ = Stimulant Craving Questionnaire.
*P-value < 0.05, **P-value < 0.01, ***P-value < 0.001

Discussion

This study documents factors related to psychotic and depressive symptoms in a cohort of methamphetamine users. Although the longitudinal course of symptoms was not the aim of this study, it is clear that a remarkable number of factors may predict methamphetamine-related positive psychotic and affective symptoms.

Methamphetamine users have been reported to have reduced dopamine transmission, which itself may play a part in suicide attempts (39, 40). Studies suggest that individuals with methamphetamine use have almost five times higher likelihood of attempting suicide in comparison with control groups (41, 42).

We found that the loss of insight and suicide attempts were associated with higher SAPS scores. Aligned with previous studies in the literature, severe positive symptoms demonstrate frequent relapses, suicide attempts, lack of treatment retention, hospital readmissions, and worse outcomes (43, 44). These results indicate that patients with low insight and a history of suicide attempts are at an increased risk for psychosis.

Consistent with the findings in the literature, we also found a positive relation between the amount of methamphetamine used and SAPS scores (10, 45-48). In a systematic review, a few studies that reported no association were considered vulnerable to selection and recall bias (49).

In contrast to studies reporting no association between psychosis and employment status, our study revealed that working with family members was negatively associated with psychotic symptoms. Although intimate relationships with family members has been reported as a protective factor in previous studies, this study may be the first study reporting an association in terms of employment status, among the studies conducted so far (6, 48, 50-52).

Although craving severity was not found to be related to psychosis severity, cessation symptoms strongly predicted psychotic symptoms. In a previous study, it was shown that the more severe the withdrawal stage, the more pronounced the psychotic symptoms experienced by patients (48). Although all clinical scales, except for the craving scale, were associated with

SAPS scores, the CGI and SAI-E scores remained significantly associated after adjusting for all variables. As reported in previous studies, clinical severity assessment of illness (CGI scores) was associated with SAPS scores (52).

Methamphetamine abuse has been associated with "high" feelings and enhancement in mood, while withdrawal symptoms included depressive symptoms, fatigue, malaise, and inactivity (53). Thus, depressive symptoms may be related to chronic use and subsequent withdrawal. (14, 48). In Zweben's study, psychological symptoms including depression subscales were significantly higher among those reporting more frequent and higher amount of methamphetamine use (17). In our study, the amount of methamphetamine use predicted higher MADRS scores. Furthermore, in a recent study, symptoms exacerbated by methamphetamine use were reported to cluster on three dimensions, with anxiety as a main element of affective dimension. (11). Therefore, the data in our study support the coexistence of anxiety (as assessed by HARS) and depressive symptoms in methamphetamine users. Depressive symptoms seem to accompany suicidal thoughts and decreased quality of life (54-57). Consistent with these results, we found out that having suicide attempts and the number of suicide attempts were significantly associated with depressive symptoms in individuals who use methamphetamine. It is important to note that depressive symptoms form an important cluster of withdrawal symptoms, which is why the ACSA scores predicted depressive symptoms, as expected. However, the SAPS scores were negatively associated with the MADRS scores, because of varying results between the two analyses, and thus, this association should be interpreted with caution.

Limitation

This study has several limitations that should be considered. First, methamphetamine use variables such as the amount, frequency and total duration of use were self-reported by the participants; thus, confirmation by family members or past treatment history could contribute to more accurate results. Second, the heterogeneity of the sample may have influenced the results. By defining abstinent patients and active users as separate groups or recording the duration between the last methamphetamine use and the interview in future studies, confounding results may be decreased. Moreover, the urine toxicology results were used to limit the effect of period in this study; however, the urine results may only provide information about the last time of methamphetamine use to a certain extent. Third, although restrictive inclusion criteria eliminated the effects of polydrug use, conducting a study with higher population may further underscore previous findings. Finally, we could not evaluate the temporal course of symptoms and family history of psychotic and depressive disorders in this study.

Conclusion

To conclude, assessing depressive and psychotic symptoms in individuals with methamphetamine use is a unique factor to provide effective treatments. The findings of this study suggest that suicide may be a strong predictor of both depressive and psychotic symptoms. A thorough evaluation of suicide at admission seems to be important in methamphetamine users. Harm reduction efforts need to target methamphetamine-associated psychotic patients who have lost insight because they may be at an elevated risk of hospitalization and antipsychotic treatment needs. Patients who were prescribed psychotropic medications must be assessed in terms of their level of insight due to potential medication nonadherence. The amount of methamphetamine used by individuals also seems to be a predictor of both depressive and psychotic symptoms. Chronic binge smoker subgroups in methamphetamine users may be at risk of both substance-related depression and psychosis. This study provides significant contribution to the literature on the methamphetamine use characteristics in Turkey, and will impart a clearer understanding to formulate an effective management of the related symptoms. Despite growing evidence in the literature, further research including prospective studies is needed.

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Conflict of Interest

None.

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