Anxiety symptoms in Chinese people who use methamphetamine: Prevalence, demographics, and clinical characteristic

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Abstract

Background

Anxiety is a common comorbidity during methamphetamine withdrawal. However, few studies have investigated comorbid anxiety in methamphetamine-dependent patients in the Chinese population. The main purpose of this study was to explore the prevalence and factors associated with comorbid anxiety during withdrawal in Chinese male methamphetamine-dependent individuals.

Methods

In this cross-sectional study, we recruited 802 methamphetamine use patients from a drug rehabilitation center in China and collected general and sociodemographic information. For all participants, we used the Beck Anxiety Inventory (BAI) self-report scale to assess anxiety symptoms, the Desire for Drug Questionnaire (DDQ) to assess drug craving, and the Pittsburgh Sleep Quality Index (PSQI) to assess sleep quality.

Results

The prevalence of comorbid anxiety symptoms in MA use patients was 19.7% (157/796). Chi-square test showed significant differences in suicidal ideation, smoking, craving, and sleep disturbances between MA use patients with and without anxiety symptoms (all p < 0.05). Furthermore, binary logistic regression revealed that suicidal ideation, drug craving, and sleep disturbances were associated with anxiety symptoms in MA use patients (all p < 0.05). Correlation analysis demonstrated that anxiety symptoms were positively associated with suicidal ideation, withdrawal period, and drug craving, but negatively with sleep quality (all p < 0.05). Stepwise multiple regression analysis indicated that suicidal ideation, withdrawal period, drug craving, and sleep quality remained significantly associated with the severity of anxiety symptoms.

Conclusion

Our results indicate a relatively higher prevalence of comorbid anxiety in Chinese MA use patients. Some sociodemographic and clinical variables are associated with comorbid anxiety in MA use patients during withdrawal.

1. Introduction

Over the past few decades, China has become one of the largest markets for Methamphetamine (MA) and a growing producer worldwide [1]. MA is a highly addictive and widely abused substance that can lead to serious physical, cognitive, and emotional consequences [2–4]. Also, people with substance use disorder (SUD) are significantly more likely to develop other psychiatric disorders, such as anxiety [5]. Anxiety symptoms in MA use patients are associated with increased relapse, low treatment adherence, and poorer life outcomes [6]. Anxiety is also a core symptom of MA withdrawal, along with symptoms such as depression, poor sleep quality, and craving [7]. Although there have been studies on the co-occurrence of anxiety and addiction mechanisms [8, 9], the nature of the comorbidity is still poorly understood, thus leaving an important knowledge gap.

Suicide risk is another serious outcome of SUD that harms individuals, families, and societies. Substance use is associated with elevated suicide ideation, suicide attempt and suicide deaths [10]. On the other hand, anxiety disorders are also positively associated with suicidal behaviors [11]. Therefore, determining the role of suicide risk in comorbid substance use and anxiety is essential for developing early detection, prevention, and treatment strategies.

According to the DSM-5, craving has emerged as a major diagnostic feature of addiction [12]. It is a crucial indicator in predicting concurrent and prospective substance use and a central determinant of relapse [13]. Craving has been identified as a mediator of substance use in people with comorbid anxiety disorders. For example, an ecological momentary assessment study in France has shown that MA users with anxiety symptoms have higher craving intensity as well as escalated substance use, although the more frequent substance use is partly independent of craving [14]. It may be meaningful to predict withdrawal and relapse with craving measures and to identify craving as a target for intervention.

EEG and circadian rhythm analyses have demonstrated that substance use affects sleep physiology, particularly the neurotransmitter systems involved in the sleep-wake system. Moreover, sleep quality may interact with addiction: early substance use may lead to sleep disturbance, which in turn increases substance use and leads to addiction [15]. Sleep disturbance predicts SUD outcomes; baseline sleep disturbance is associated with worse outcomes, mediated by mood and craving [16]. Anxiety sensitivity, i.e., responsiveness to physiological arousal from perceived danger, has been shown to contribute to low sleep quality in SUD subjects with anxiety disorders [17]. Therefore, focusing on sleep disturbances when examining the co-morbidity of MA use and anxiety symptoms may provide a new perspective to explain the link between them.

There are no systematic studies on the role and risk factors of anxiety among MA use patients in China. Therefore, the aim of this study was to investigate the prevalence and clinical correlates of comorbid anxiety symptoms in Chinese MA use patients, particularly the relationship with suicide risk, craving, and sleep disturbance. We hypothesized that (1) the prevalence of anxiety symptoms would be higher in MA use patients than in the general Chinese population; (2) some demographic and clinical variables, especially suicide risk, craving, and sleep disturbance would be positively associated with anxiety symptoms in MA use patients. In addition, gender is a critical demographic determinant of SUD behaviors, and there is gender differences in the prevalence and risk factors of SUD [18]. We focused on male MA use patients in this study.
2. Methods

2.1. Subjects

This cross-sectional study was conducted at a drug rehabilitation center in Mianyang City, Sichuan Province, China. Participants were recruited consecutively between November 2020 and July 2021. A total of 802 eligible participants were recruited. Those included in this study had to meet the following inclusion criteria: (1) age ≥ 18 years old and Han Chinese; (2) MA-only users with positive urine tests upon admission to the drug rehabilitation center; (3) meeting the Diagnostic and Statistical Manual of Mental Disorders (DSM) 5th edition criteria for MA use patients; and (4) excluding subjects who were dependent on other drugs or had other serious brain and physical diseases.

The study was approved by the Ethics Committee of the Institute of Psychology, Chinese Academy of Sciences and was conducted in accordance with the Declaration of Helsinki. All enrolled patients were fully explained and provided written informed consent before participating in this study.

2.2. Data collection and assessment

Sociodemographic information was collected for all participants: including gender, age, education, marital status, BMI, smoking and alcohol use, as well as MA use information, including duration of MA use, age of first use, dose of MA use and withdrawal period. In particular, we collected information on suicide among patients. In addition, we collected a complete medical history of all participants and performed physical examinations and laboratory tests. Subjects with physical illness were excluded.

We used the Beck Anxiety Inventory (BAI) self-report scale to assess anxiety symptoms in MA use patients. The scale focuses on somatic symptoms of anxiety and has 21 items. Responses are based on a 4-point Likert scale ranging from 0 (not at all) to 3 (severe), with a maximum total score of 63. A score of ≤ 21 indicates low anxiety, 22–35 indicates moderate anxiety, and 36 or more indicates high anxiety[19].

The Desire for Drug Questionnaire (DDQ) is used to measure an patient's current craving for drugs. The scale consists of three dimensions: desire and intention, negative reinforcement, and control. Of these, the desire and intention dimension measures the subject’s desire for drugs, the negative reinforcement dimension measures the subject's thoughts about using drugs to reduce negative states, and the control dimension measures the subject’s self-control. Higher scores on the Desire and Intention and Negative Reinforcement dimensions indicate higher desire for MA, whereas higher score on the Control dimension indicate that the subject has better control over MA cravings[20].

The Pittsburgh Sleep Quality Index scale (PSQI) was used to measure the quality of sleep in the most recent month. It includes 7 dimensions: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency and sleep disorders, sleep medication use, and daytime dysfunction. The total score of PSQI is 7 dimensions added together. Higher score indicates poorer sleep quality. A score of 0–5 is good sleep quality, 6–10 is average sleep quality, 11–15 is fair sleep quality, and 16–21 is very poor sleep quality[21].

Prior to the start of the study, two psychiatrists with at least 5 years of experience in clinical practice attended training in the use of the BAI, DDQ and PSQI. At the end of the training, the inter-rater correlation coefficients for the total scores of the BAI, DDQ and PSQI were greater than 0.8.

2.3. Statistical analysis

We first conducted descriptive analyses of demographic and clinical parameters of MA use patients with and without anxiety symptoms, and the prevalence of anxiety symptoms in MA use patients was described as a percentage. Second, we compared demographic and clinical parameters of MA use patients with and without anxiety symptoms. All demographic and clinical variables for MA use patients with and without anxiety symptoms were normally distributed (Kolmogorov-Smirnov one-sample test, all P > 0.05). Continuous data were analyzed by analysis of variance (ANOVA) and categorical data by chi-square test to compare the differences in demographic and clinical variables between the two groups. Correlations between demographic and clinical variables were tested with Pearson correlation coefficients. In addition, binary logistic regression analyses and multiple linear regression analyses were performed to assess which factors were most strongly associated with anxiety symptoms in MA use patients.

All data were statistically analyzed using SPSS 21.0, and the strength of correlations was quantified using coefficient values, odds ratios (ORs), and 95% confidence intervals (CIs). Statistical significance was established at p < 0.05.

3. Results

3.1. Prevalence of MA use patients with anxiety symptoms

A total of 802 MA use patients were included in this study. In the entire sample group, the prevalence of anxiety symptoms was 19.7% (157/796), showing mild anxiety symptoms of 14.1% (112/796), moderate anxiety symptoms of 4.1% (33/796), and severe anxiety symptoms of 1.5% (33/796).

3.2 Comparison of the clinical characteristics between MA use patients with and without anxiety symptoms

Table 1 summarizes the differences in demographic and clinical characteristics of patients with (n = 639) and without anxiety symptoms (n = 157). The chi-square test showed significant differences between groups in suicidal ideation and suicidal behavior ($\chi^2 = 23.81, df = 1, P < 0.001$) and smoking ($\chi^2 = 5.95, df = 2, P = 0.051$). Compared to patients without anxiety, patients with anxiety symptoms had higher total DDQ scores (F = 16.16, P = 0.001), total PSQI scores (F = 31.01, P < 0.001), and their subscales (all P < 0.05). However, there were no significant differences between the two groups in terms of age, education, and substance use information including duration of use, age of first use, dose of use and withdrawal period (all P > 0.05).
Table 1
demographic and clinical characteristics in MA use patients with and without anxiety symptoms

<table>
<thead>
<tr>
<th></th>
<th>Total patients (N = 802)</th>
<th>Patients without anxiety (n = 639)</th>
<th>Patients with anxiety (n = 157)</th>
<th>F</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(years)</td>
<td>34.21 ± 6.76</td>
<td>34.20 ± 6.82</td>
<td>34.21 ± 6.54</td>
<td>0.00</td>
<td>0.991</td>
</tr>
<tr>
<td>years of education(years)</td>
<td>9.43 ± 2.29</td>
<td>9.41 ± 2.31</td>
<td>9.48 ± 2.20</td>
<td>0.10</td>
<td>0.756</td>
</tr>
<tr>
<td>BMI(kg/m²)</td>
<td>24.14 ± 3.23</td>
<td>24.15 ± 3.24</td>
<td>24.11 ± 3.19</td>
<td>0.02</td>
<td>0.893</td>
</tr>
<tr>
<td>Duration of MA use(months)</td>
<td>101.52 ± 47.29</td>
<td>101.81 ± 47.72</td>
<td>100.31 ± 45.62</td>
<td>0.13</td>
<td>0.724</td>
</tr>
<tr>
<td>Age of first MA use(years)</td>
<td>24.53 ± 7.16</td>
<td>24.54 ± 7.20</td>
<td>24.46 ± 7.01</td>
<td>0.02</td>
<td>0.904</td>
</tr>
<tr>
<td>Dose of MA use(g)</td>
<td>1413.44 ± 2954.50</td>
<td>1384.78 ± 2839.75</td>
<td>1532.26 ± 3397.03</td>
<td>0.30</td>
<td>0.582</td>
</tr>
<tr>
<td>Withdrawal period(months)</td>
<td>14.75 ± 6.40</td>
<td>14.95 ± 6.39</td>
<td>13.95 ± 6.39</td>
<td>2.95</td>
<td>0.086</td>
</tr>
<tr>
<td>DDQ total score</td>
<td>6.65 ± 3.04</td>
<td>6.44 ± 2.95</td>
<td>7.52 ± 3.23</td>
<td>16.16</td>
<td>0.000***</td>
</tr>
<tr>
<td>desire and intention</td>
<td>1.70 ± 0.92</td>
<td>1.61 ± 0.85</td>
<td>2.04 ± 1.12</td>
<td>27.48</td>
<td>0.000***</td>
</tr>
<tr>
<td>negative reinforcement</td>
<td>1.88 ± 1.171</td>
<td>1.78 ± 1.12</td>
<td>2.27 ± 1.31</td>
<td>22.39</td>
<td>0.000***</td>
</tr>
<tr>
<td>control</td>
<td>3.07 ± 1.79</td>
<td>3.04 ± 1.82</td>
<td>3.21 ± 1.67</td>
<td>1.06</td>
<td>0.304</td>
</tr>
<tr>
<td>PSQI total score</td>
<td>8.11 ± 6.17</td>
<td>7.36 ± 5.74</td>
<td>11.36 ± 6.92</td>
<td>31.01</td>
<td>0.000***</td>
</tr>
<tr>
<td>subjective sleep quality</td>
<td>0.94 ± 0.74</td>
<td>0.85 ± 0.69</td>
<td>1.33 ± 0.81</td>
<td>31.39</td>
<td>0.000***</td>
</tr>
<tr>
<td>sleep latency</td>
<td>1.10 ± 0.93</td>
<td>1.02 ± 0.89</td>
<td>1.45 ± 1.03</td>
<td>14.71</td>
<td>0.000***</td>
</tr>
<tr>
<td>sleep duration</td>
<td>0.60 ± 0.72</td>
<td>0.53 ± 0.67</td>
<td>0.89 ± 0.82</td>
<td>18.32</td>
<td>0.000***</td>
</tr>
<tr>
<td>habitual sleep efficiency</td>
<td>0.37 ± 0.67</td>
<td>0.34 ± 0.62</td>
<td>0.51 ± 0.84</td>
<td>3.87</td>
<td>0.050*</td>
</tr>
<tr>
<td>sleep disturbance</td>
<td>0.78 ± 0.42</td>
<td>0.76 ± 0.43</td>
<td>0.86 ± 0.35</td>
<td>2.53</td>
<td>0.113</td>
</tr>
<tr>
<td>use of sleeping medication</td>
<td>0.02 ± 0.13</td>
<td>0.01 ± 0.11</td>
<td>0.05 ± 0.21</td>
<td>5.14</td>
<td>0.024</td>
</tr>
<tr>
<td>daytime dysfunction</td>
<td>1.42 ± 0.95</td>
<td>1.31 ± 0.91</td>
<td>2.00 ± 0.92</td>
<td>23.23</td>
<td>0.000***</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>married</td>
<td>223(28.16%)</td>
<td>179(28.10%)</td>
<td>44(28.39%)</td>
<td>0.42</td>
<td>0.98</td>
</tr>
<tr>
<td>unmarried</td>
<td>320(40.40%)</td>
<td>257(40.35%)</td>
<td>63(40.65%)</td>
<td>0.01</td>
<td>0.941</td>
</tr>
<tr>
<td>divorced</td>
<td>240(30.15%)</td>
<td>194(30.46%)</td>
<td>46(29.68%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>widowed</td>
<td>1(0.13%)</td>
<td>1(0.16%)</td>
<td>0(0%)</td>
<td>5.95</td>
<td>0.051</td>
</tr>
<tr>
<td>cohabiting</td>
<td>8(1.01%)</td>
<td>6(0.94%)</td>
<td>2(1.30%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drinking history</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>never drinker</td>
<td>526(66.41%)</td>
<td>422(66.35%)</td>
<td>104(66.675%)</td>
<td>0.01</td>
<td>0.941</td>
</tr>
<tr>
<td>former drinker</td>
<td>266(33.59%)</td>
<td>214(33.65%)</td>
<td>52(33.33%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking history</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>never smoker</td>
<td>10(1.26%)</td>
<td>10(1.57%)</td>
<td>0(0%)</td>
<td>4(2.56%)</td>
<td>0.051</td>
</tr>
<tr>
<td>former smoker</td>
<td>9(1.13%)</td>
<td>5(0.78%)</td>
<td>4(2.56%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>current smoker</td>
<td>774(97.60%)</td>
<td>622(97.65%)</td>
<td>152(97.46%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suicide</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>never suicide</td>
<td>727(92.03%)</td>
<td>600(94.34%)</td>
<td>127(82.47%)</td>
<td>23.81</td>
<td>0.000***</td>
</tr>
<tr>
<td>suicide ideation</td>
<td>63(7.97%)</td>
<td>36(5.66%)</td>
<td>27(17.53%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: BMI = body mass index, DDQ = Desire for Drug Questionnaire, PSQI = Pittsburgh Sleep Quality Index Scale.

The significance of bold emphases in the table is p < 0.05.

*P < 0.05; **P < 0.01; ***P < 0.001.

3.3. The factors related to anxiety symptoms in MA use patients
As shown in Table 2, we used binary logistic regression to assess the effects of demographic and clinical parameters on anxiety symptoms in MA use patients. The results showed that the following variables were independently associated with anxiety symptoms: presence of suicidal ideation and suicidal behavior (Wald $\chi^2 = 12.16$, OR = 0.29, 95% CI 0.14–0.58, df = 1, $p < 0.001$), drug craving (Wald $\chi^2 = 4.20$, OR = 1.09, 95% CI 1.00–1.18, df = 1, $p = 0.040$), and presence of sleep disturbance (Wald $\chi^2 = 23.01$, OR = 1.10, 95% CI 1.06–1.14, df = 1, $p < 0.001$), showing that for each unit increase in total PSQI score, the likelihood of increased anxiety in MA use patients was 9.5%.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Coefficients</th>
<th>Std.error</th>
<th>Wald</th>
<th>P value</th>
<th>95% confidence interval for EXP (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(constant)</td>
<td>-1.76</td>
<td>0.48</td>
<td>13.72</td>
<td>0.000***</td>
<td>0.17</td>
</tr>
<tr>
<td>suicide</td>
<td>-1.25</td>
<td>0.36</td>
<td>12.16</td>
<td>0.000***</td>
<td>0.29, 0.14, 0.58</td>
</tr>
<tr>
<td>DDQ total score</td>
<td>0.08</td>
<td>0.04</td>
<td>4.20</td>
<td>0.040*</td>
<td>1.09, 1.00, 1.18</td>
</tr>
<tr>
<td>PSQI total score</td>
<td>0.09</td>
<td>0.02</td>
<td>23.01</td>
<td>0.000***</td>
<td>1.10, 1.06, 1.14</td>
</tr>
</tbody>
</table>

Note: DDQ = Desire for Drug Questionnaire, PSQI = Pittsburgh Sleep Quality Index Scale.

As shown in Table 3, Pearson correlation analysis revealed significant correlations between the total BAI score and the following parameters: suicide ideation and suicidal behavior ($r = 0.18$, df = 788, $p < 0.001$), withdrawal period ($r = 0.10$, df = 767, $p = 0.005$), DDQ total score ($r = 0.16$, df = 787, $p < 0.001$) and its Desire and Intention and Negative Reinforcement subscales (both $r = 0.18$, df = 786, $p < 0.001$), as well as PSQI total ($r = 0.31$, df = 453, $p < 0.001$) and its subscale scores ($r = 0.12–0.33$, df = 453, $p < 0.017–0.001$).
Table 3
Inter-relationships between demographic and clinical variables in MA use patients

<table>
<thead>
<tr>
<th>variables</th>
<th>BAI</th>
<th>suicide</th>
<th>withdrawal period(years)</th>
<th>DDQ total score</th>
<th>DDQ desire and intention</th>
<th>DDQ negative reinforcement</th>
<th>DDQ control</th>
<th>PSQI total score</th>
<th>PSQI subjective sleep quality</th>
<th>PSQI sleep latency</th>
<th>PSQI sleep duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAI</td>
<td>1</td>
<td>0.000***</td>
<td>0.005**</td>
<td>0.000***</td>
<td>0.000***</td>
<td>0.000***</td>
<td>0.102</td>
<td>0.000***</td>
<td>0.000***</td>
<td>0.000***</td>
<td>0.000***</td>
</tr>
<tr>
<td>suicide</td>
<td>0.018**</td>
<td>1</td>
<td>0.0106</td>
<td>0.006**</td>
<td>0.053</td>
<td>0.000***</td>
<td>0.674</td>
<td>0.019*</td>
<td>0.417</td>
<td>0.656</td>
<td>0.102</td>
</tr>
<tr>
<td>withdrawal period(years)</td>
<td>-0.10**</td>
<td>0.06</td>
<td>1</td>
<td>0.078</td>
<td>0.974</td>
<td>0.455</td>
<td>0.016*</td>
<td>0.000***</td>
<td>0.078</td>
<td>0.376</td>
<td>0.602</td>
</tr>
<tr>
<td>DDQ total score</td>
<td>0.16**</td>
<td>0.10**</td>
<td>-0.06</td>
<td>1</td>
<td>0.000***</td>
<td>0.000***</td>
<td>0.000***</td>
<td>0.024*</td>
<td>0.501</td>
<td>0.044*</td>
<td>0.059</td>
</tr>
<tr>
<td>DDQ desire and intention</td>
<td>0.18**</td>
<td>0.07</td>
<td>0.00</td>
<td>0.79**</td>
<td>1</td>
<td>0.000***</td>
<td>0.000***</td>
<td>0.014*</td>
<td>0.832</td>
<td>0.115</td>
<td>0.032*</td>
</tr>
<tr>
<td>DDQ negative reinforcement</td>
<td>0.18**</td>
<td>0.18**</td>
<td>-0.03</td>
<td>0.75**</td>
<td>0.70**</td>
<td>1</td>
<td>0.000***</td>
<td>0.073</td>
<td>0.165</td>
<td>0.048*</td>
<td>0.030*</td>
</tr>
<tr>
<td>DDQ control</td>
<td>0.06</td>
<td>0.02</td>
<td>-0.09*</td>
<td>0.80**</td>
<td>0.36**</td>
<td>0.24**</td>
<td>1</td>
<td>0.185</td>
<td>0.977</td>
<td>0.218</td>
<td>0.537</td>
</tr>
<tr>
<td>PSQI total score</td>
<td>0.31**</td>
<td>0.06</td>
<td>-0.43**</td>
<td>0.11*</td>
<td>0.12*</td>
<td>0.09</td>
<td>0.06</td>
<td>1</td>
<td>0.000***</td>
<td>0.000***</td>
<td>0.000***</td>
</tr>
<tr>
<td>PSQI subjective sleep quality</td>
<td>0.33**</td>
<td>0.04</td>
<td>-0.09</td>
<td>0.03</td>
<td>0.01</td>
<td>0.07</td>
<td>0.00</td>
<td>0.38**</td>
<td>1</td>
<td>0.000***</td>
<td>0.000***</td>
</tr>
<tr>
<td>PSQI sleep latency</td>
<td>0.23**</td>
<td>0.02</td>
<td>-0.04</td>
<td>0.10*</td>
<td>0.07</td>
<td>0.09*</td>
<td>0.06</td>
<td>0.36**</td>
<td>0.39**</td>
<td>1</td>
<td>0.000***</td>
</tr>
<tr>
<td>PSQI sleep duration</td>
<td>0.26**</td>
<td>0.08</td>
<td>-0.03</td>
<td>0.09</td>
<td>0.10*</td>
<td>0.10*</td>
<td>0.03</td>
<td>0.22**</td>
<td>0.26**</td>
<td>0.27**</td>
<td>1</td>
</tr>
<tr>
<td>PSQI habitual sleep efficiency</td>
<td>0.12*</td>
<td>-0.00</td>
<td>-0.05</td>
<td>0.04</td>
<td>0.07</td>
<td>0.04</td>
<td>0.01</td>
<td>0.17**</td>
<td>0.20**</td>
<td>0.21**</td>
<td>0.65**</td>
</tr>
<tr>
<td>PSQI sleep disturbance</td>
<td>0.17**</td>
<td>0.11*</td>
<td>-0.06</td>
<td>0.10*</td>
<td>0.08</td>
<td>0.08</td>
<td>0.08</td>
<td>0.34**</td>
<td>0.27**</td>
<td>0.22**</td>
<td>0.17**</td>
</tr>
<tr>
<td>PSQI use of sleeping medication</td>
<td>0.19**</td>
<td>-0.04</td>
<td>-0.05</td>
<td>0.01</td>
<td>0.07</td>
<td>0.01</td>
<td>-0.04</td>
<td>0.12*</td>
<td>0.26**</td>
<td>0.02</td>
<td>0.05</td>
</tr>
<tr>
<td>PSQI daytime dysfunction</td>
<td>0.33**</td>
<td>0.06</td>
<td>-0.14*</td>
<td>0.00</td>
<td>0.02</td>
<td>0.01</td>
<td>-0.02</td>
<td>0.37**</td>
<td>0.31**</td>
<td>0.21**</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Note: BAI = Beck Anxiety Inventory; DDQ = Desire for Drug Questionnaire; PSQI = Pittsburgh Sleep Quality Index Scale.

diagonal elements of correlation matrix, correlations coefficients between the possible pairs of variables are shown. In the right side of the diagonal elements correlation coefficients are shown.

*P < 0.05; **P < 0.01; ***P < 0.001.

Further multiple linear regression analysis revealed that the following variables were independently associated with the severity of anxiety symptoms in MA use patients, including suicidal ideation and suicidal behavior (B = 2.58, t = 2.86, p = 0.004), intensity of drug craving (B = 0.22, t = 2.55, p = 0.011) and severity of sleep disturbance (B = 0.28, t = 6.32, p < 0.001).

4. Discussion

To our knowledge, the present study is the first to examine the prevalence and clinical factors associated with anxiety symptoms in a large sample of male MA use patients in the Chinese Han population. The main findings of our study were as follows: (1) The prevalence of anxiety symptoms in Chinese male MA use patients was 17.9%; and (2) several demographic and clinical variables were associated with anxiety symptoms, including suicidal thoughts, drug cravings, and severe sleep disturbances.

Limited information is available regarding the prevalence of anxiety symptoms associated with MA use. In our sample, the prevalence of anxiety symptoms was lower than that reported in studies in western countries such as the United States and Australia[5, 22–24], but significantly higher than the 7% reported in South Africa [25]. In a research project on outpatient treatment of MA dependence in gay and bisexual men, 25% of MA users reported a lifetime prevalence of drug-induced anxiety disorders[26]. The prevalence of anxiety symptoms varies from country to country, possibly due to differences in economy, quality and environment of health care, and national policies. Differences in methodology, sample selection, and size among studies may also contribute.

Two studies have been conducted among local Chinese MA use patients. One study enrolled 1,685 MA-based drug users in drug rehabilitation centers in Beijing and Guangzhou and reported a 29.06% prevalence of anxiety symptoms[27]. This rate is higher than ours and may be due to the economic and life stressors in the subjects’ areas. Another cross-sectional study reported that 34.3% of MA use patients had anxiety level during acute withdrawal (1–7 days from last drug use)[28]. The higher level of anxiety during acute withdrawal could well be explained by our findings in this study, which showed a significant
negative correlation between anxiety symptoms and the length of withdrawal, implying that anxiety levels were higher in the early stages of withdrawal, and as the duration of withdrawal increased, patients gradually adapted thereby decreasing their anxiety levels.

Further, the present study found that MA use patients with suicidal thoughts were more likely to be diagnosed with anxiety symptoms than those without suicidal thoughts, which is consistent with previous research that individuals with anxiety disorders are at increased risk for suicide[29]. The relationship between anxiety symptoms and suicide appears to be well established, with anxiety being listed as a significant risk factor for suicide by several national organizations [30, 31]. However, most of the existing literature is cross-sectional, which only suggests that suicidal thoughts are a correlate of anxiety symptoms[32, 33]. Furthermore, the current literature examining anxiety symptoms and suicidal thoughts in drug-addicted patients is limited. A prospective six-year follow-up study of suicide attempts in drug-dependent patients reported that the frequency of suicide in drug use patients or during withdrawal remained high compared to the suicide rate in the general population. However, in contrast to our present study, they found a reduced risk of suicide in individuals with lifelong generalized anxiety disorder [34]. In addition, a 3-year post-treatment follow-up of MA users with anxiety disorders found that people with anxiety disorders were more than three times as likely to attempt suicide one or more times in their lifetime than those without anxiety disorders [22], which is consistent with the present study. According to Beck's cognitive model of suicide, a number of life stressors activate suicidal patterns, and anxiety symptoms, as an emotional and behavioral manifestation of attention fixation, interacts with feelings of hopelessness as a solution to relieve stress, thereby exacerbating suicidal ideation [35].

Drug craving may also well explain high anxiety symptoms and suicidal ideation. The present study found that drug craving was a predictor of anxiety levels in MA use patients, which is also consistent with previous research on other SUD populations [36, 37]. The temporal priority of anxiety symptoms and craving emergence is currently controversial. Some studies suggest that changes in anxiety symptoms precede and predict subsequent changes in craving, and that individuals with anxiety disorders may crave more substances to alleviate current negative emotions [38]. In contrast, the motivational dimension model of affect suggests that individuals with strong drug cravings exhibit high levels of approach motivation, which tends to induce positive emotions and focus the individual's attention on the goal of obtaining drugs [39]. However, when drug use patients in rehabilitation centers develop a strong drug craving but are unable to obtain drugs, this high convergent motivation generates more anxiety and the accumulation of negative emotions may lead to suicide. Furthermore, a negatively reinforced model of affective processing suggests that avoidance of negative emotions motivates individuals to maintain addictive behaviors [40]. Patients avoid bad emotions by engaging in more substance abuse behaviors, and substance use leads to feelings of euphoria and well-being, alleviating the unpleasant experiences associated with negative emotions [40]. This negatively reinforces the addictive behavior, which in turn triggers higher levels of anxiety symptoms, creating a vicious cycle. A growing body of research supports the competing hypothesis that the interaction between mood states and substance use states is bidirectional [37].

Sleep disorders as a side effect of MA addiction also have a significant impact on anxiety symptoms. This study found that patients with sleep disorders were more likely to have comorbid anxiety symptoms, which is consistent with the results of numerous studies showing an association between sleep disorders and anxiety symptoms [41–43]. The disruptive effects of MA on sleep are caused by altered levels and activity of dopamine, which is known to play an important role in regulating the sleep-wake cycle [44], and damage to dopaminergic neurons can cause anxiety symptoms [45]. Several studies have shown that anxiety symptoms are associated with disruptions in rapid eye movement sleep [46], often accompanied by dysregulation of substances such as norepinephrine, dopamine, and serotonin [47]. MA reduces the duration of the rapid eye movement period and prolongs sleep latency and wakefulness through these monoamines [48], resulting in greater daytime sleepiness in individuals with poor sleep quality [49]. In this study, we found that the daytime dysfunction sub-dimension had the greatest impact on anxiety symptoms in MA use patients, which is consistent with the above findings. In addition, sleep can also influence drug cravings and anxiety levels through dreams. A recent study of patients with opioid use disorder (OUD) reported that recalling drug-related dreams from the past week may report more sleep disturbances, including poorer sleep quality, and more severe insomnia symptoms. Substantial increases in drug cravings following dreams have been associated with greater anxiety symptoms [50]. Sleep duration and disorders can affect anxiety symptoms, and similarly, increased anxiety level can negatively affect sleep; for example, excessive worry about insomnia may exacerbate sleep disturbances [51]. However, the psychological mechanisms of anxiety are unclear, and research on anxiety in MA use patients is still in its infancy and further research is needed.

Several limitations of the present study are noteworthy. First, the comorbidity of anxiety and depression is very common, which was not broken down in the present study. It is possible that some patients have symptoms of both anxiety and depression. Second, we were unable to distinguish whether anxiety symptoms occurred prior to or was caused by drug use. Third, this was a cross-sectional study, so it was not possible to determine a causal relationship between anxiety symptoms and other factors. Fourth, this study only included male subjects, and a recent study has reported a higher incidence of anxiety in women [5]. Therefore, further research should explore gender differences in anxiety in MA use patients. Fifth, there are many genetic and environmental factors that may influence anxiety symptoms, such as genetic susceptibility, personality traits, and social support. However, these data were not collected in this study, and further controlled studies should be conducted to demonstrate the relationship between these factors and anxiety symptoms.

In conclusion, the current study showed that the prevalence of anxiety symptoms among MA use patients was 17.9%, indicating that anxiety symptoms are common among MA use patients in the Chinese Han population. Furthermore, our study showed a significant negative correlation between anxiety symptoms and the duration of MA withdrawal, implying that anxiety may subside with increasing withdrawal time. Our study further suggests that related factors for anxiety symptoms are suicidal ideation, drug craving, and sleep disturbance. Understanding the risk factors for anxiety symptoms will provide important implications for prevention and intervention to reduce the psychological burden of MA addiction.

**Declarations**

**Conflict of Interest**

No conflict of interest was disclosed for each author.
Role of the Funding Source

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Data statement

The data that support the findings of this study are available on request from the corresponding author.

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