RESEARCH

Prevalence of anxiety disorders and its co-occurrence with substance use disorder: a clinical study

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Abstract

Background: Epidemiological studies are necessary to develop diagnostic standards for mental disorders. Therefore, this study investigated the prevalence of anxiety disorders, and its correlation with different substances used by patients diagnosed with substance use disorder referred to the Iran Psychiatric Hospital located in Tehran, Iran. Two hundred ninety-two male patients aged 18–65 (Mean$_{age}$ = 36.11, SD = 10.55) were recruited according to the available participant pool. Structured Clinical Interview for DSM-V Axis I Disorders was used to investigate their simultaneous anxiety disorders, and then the correlations with the different substances used during the past year before our study were considered. Based on clinical evaluation and structured psychiatric interviews, we investigated panic disorder, agoraphobia, social anxiety disorder, and generalized anxiety disorder.

Results: Results revealed that generalized anxiety disorder was the most common type of anxiety disorder among subjects of the current study. Further investigations revealed that panic disorder was significantly correlated with the abuse of cannabis ($r = 0.116$, p value = 0.047), tramadol ($r = 0.205$, p value < 0.001), and LSD ($r = 0.197$, p value = 0.001). Moreover, social anxiety disorder was correlated with cannabis ($r = 0.124$, p value = 0.035), opium ($r = 0.186$, p value = 0.001), methadone ($r = 0.152$, p value = 0.010), tramadol ($r = 0.258$, p value < 0.001), alcohol ($r = 0.133$, p value = 0.023), LSD ($r = 0.123$, p value = 0.036), and benzodiazepines ($r = 0.168$, p value = 0.004). The results indicated that none of the substances was correlated with generalized anxiety disorder as well as agoraphobia. However, agoraphobia had correlations with the intravenous injection as the main route of administration ($r = 0.174$, p value = 0.004).

Conclusions: Here this study supports the notion that co-occurrence of psychiatric disorders is relatively common and must be taken into consideration when assessing a patient and following up the treatment.

Keywords: Anxiety disorders, Substance use disorder, Clinical patients, Psychiatric disorders

Background

The development of diagnostic standards for mental disorders has been a milestone in psychiatric epidemiological studies. Over the past years, the emphasis has been highly put on the prevalence of different areas of mental disorders including mood, anxiety, and substance use disorders, and the concurrency of the related symptoms as well [25, 26, 28, 29].

Recently, researchers have shown considerable interest in surveys estimating the prevalence rate of mental disorders. The anxiety disorders comprising generalized anxiety disorder (GAD), panic disorder (with/without agoraphobia), social anxiety disorder (SAD), and specific phobias are the most common mental disorders of which the ascending trend has become a concern [5].

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However, some experts have challenged the idea of a mental health crisis that has been claimed in the past three decades and have related this issue to the change of population and research methods [4]. According to the epidemiological surveys, the lifetime prevalence of anxiety disorders has been estimated as 14.5–33.7% meaning that up to approximately one-third of individuals are affected by any kinds of anxiety disorders at least once in their life [3].

Substance use disorders bring another domain of mental health into focus. They are associated with socioeconomic issues besides health problems [7]. As much as anxiety disorders, substance use disorders are frequent according to the investigations in the USA population in which lifetime prevalence has been estimated as 14.6% [24].

One of the significant topics in this field of study is the simultaneous occurrence of mental disorders which has received attention in recent years. The most common co-existing disorders are anxiety, mood, and substance use disorders [12, 14, 30]. In many cases, the first exposure to illicit drugs occurs in adolescence [21]. This may advance towards a substance dependence accompanied by anxiety symptoms which can lead to malfunction in adulthood [11, 22]. On the other hand, some of the studies indicate that anxiety disorder is a predisposing factor for substance use disorder and the individuals suffering from anxiety are more prone to substance use and dependence in the future [13, 15, 17, 20]. Several models have been developed to explain the relationships between anxiety/mood disorders and substance abuse including "precipitation", "self-medication", and "shared vulnerability" hypotheses. According to the "precipitation" model, the process starts with substance abuse and then leads to anxiety/mood disorders. In this case anxiety/mood disorders are substance-induced. In addition, this process might happen in the opposite way as well that is called the "self-medication" model. According to this hypothesis, individuals with anxiety/mood disorders engage in substance abuse so that they can cope with the disturbing symptoms of their disorders. Both of these models suggest a causal pathway based on the temporal sequence of the disorders. Furthermore, the "shared vulnerability" model indicates that common biologic and psychosocial risk factors predispose an individual to both anxiety/mood disorders and substance use disorders simultaneously. Several studies have shown that these mechanisms can interact and produce greater effects through synergism [10, 18]. Due to the mutual cause and effect pattern, the comorbidity leads to remarkable impacts on the clinical course of the disorders and the outcome of the treatment [2, 24].

According to a study in the USA, 17.7% of the subjects with substance use disorder were diagnosed with anxiety disorders at the same time [2]. In reviewing the literature, few studies have focused on the correlations between the substance type and anxiety disorders among individuals with substance use disorder. According to a study conducted by de Matos et al. in Brazil, individuals with post-traumatic stress disorder (PTSD) and generalized anxiety disorder (GAD) were major consumers of illicit substances such as stimulants. Moreover, tobacco dependence was more prevalent in subjects with agoraphobia [6]. Other studies in Australia and Canada showed that alcohol and cannabis are among the most common substances used by individuals seeking treatment whom 70.5% were diagnosed with anxiety-related disorders [21, 27]. The Iranian Mental Health Survey revealed that opioid use disorders were the most common type of substance use disorders in the Iranian population showing significant associations with mood and anxiety-related disorders [1].

Considering the co-occurrence of anxiety disorders and substance use disorders is still crucial in mental health care. As stated above, both disorders are highly frequent and overlapping which play important roles in both individuals' quality of life and public health. This study aimed to identify the prevalence and probable associations of anxiety-related disorders with different substances used by patients with substance use disorder.

Methods

Design and sample

This cross-sectional study used a convenience sample of 292 male patients. All of the participants were between 18 and 65 years old (Mean age = 36.11, SD = 10.55) and among the outpatients referred to the Iran Psychiatric Hospital located in Tehran, Iran, from March 2020 to March 2021. To enter the survey, all of the subjects had to be primarily diagnosed with substance use disorder determined by Structured Clinical Interview for DSM-V Axis I Disorders (SCID-I) in the outpatient clinic. Moreover, initial assessments were considered to confirm that the subjects did not have any signs and symptoms regarding acute episodes of psychosis, major depressive disorder, and mania. Patients with acute signs and symptoms of psychotic and mood disorders, and with the anxiety-related symptoms being justifiable with an underlying disease or a medical condition, were excluded. In addition, it was important to ensure that none of the patients with the symptoms of substance withdrawal or intoxication at the time of interview were included in this study. By checking the medical records and asking goal-oriented questions during the interviews, the anxiety-related symptoms induced by withdrawal or intoxication

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were ruled out. Prior ethical approval was obtained from the Research Ethical Committee of Iran University of Medical Sciences to conduct this study (No. 15054). Permission was granted to use participants' data for current research by obtaining informed consent in Persian language based on the World Medical Association (WMA) Declaration of Helsinki [31]. None of the subjects refused to continue with the interviews in the middle of the project.

Procedure

After obtaining the written informed consent from the participants and the initial assessments, the principal structured interview was conducted. Demographic and social status data was gathered by utilizing a standard questionnaire. Patients' characteristics such as age, gender, marital status, level of education, financial situation, occupation, past medical and psychiatric history as well as drug, substance (including the type of substance), and alcohol use, and smoking behaviors were recorded. Participants were diagnosed with substance use disorder and anxiety disorders using the Structured Clinical Interview for DSM-V Axis I Disorders (SCID-I). SCID is a diagnostic tool that is utilized to systematically identify the DSM major diagnoses [9]. This structured interview takes approximately 1–2 h in practice. In the current study, the Persian version of SCID was administered by trained mental health professionals [23]. In this descriptive study, anxiety disorders were categorized as panic disorder (PD), agoraphobia, social anxiety disorder (SAD), and generalized anxiety disorder (GAD). The participants of this study did not suffer from obsessive compulsive disorder (OCD) and post-traumatic stress disorder (PTSD). OCD and PTSD have been removed from the anxiety disorders category in the latest edition of DSM and are classified elsewhere. Therefore, the patients suffering from these two disorders were excluded from this study at the time of interview. In addition, other medical conditions such as diabetes mellitus, thyroid disease, coronary artery disease, convulsion, human immunodeficiency virus (HIV) and hepatitis B virus (HBV), and hepatitis C virus (HCV) infections were investigated.

Statistical analyses

Data management and analyses were performed using IBM SPSS Statistics for Windows, version 27.0. (Armonk, NY: IBM Corp.). Descriptive analysis was conducted to report frequencies in various categories. General linear model and Pearson correlation coefficient (Pearson's *r*) were used to investigate the correlations between substance type and different anxiety disorders. Significance level and confidence intervals were considered 0.05 and 95.0% respectively.

Results

As can be seen in Table 1, over half of the subjects were unmarried (57.2%). Moreover, the majority of the participants had not finished high school (53.1%) and only 8.6% of them were holders of a bachelor's or a higher degree. In addition, 154 participants were unemployed (52.8%) (Table 1).

Statistical analysis showed that tobacco was the most common substance (89.4%) used by participants followed by crystal (53.8%) and heroin (49.7%) (Table 2). Furthermore, smoking (84.9%) and intravenous injection (9.6%) were the most and the least common routes of administration respectively. Comparison of the frequencies revealed that generalized anxiety disorder (GAD) was the most common type of anxiety disorder among subjects of the current study (28.4%) (Table 3).

Further investigations revealed that PD was significantly correlated with the abuse of cannabis ($r = 0.116$, *p* value = 0.047), tramadol ($r = 0.205$, *p* value < 0.001), and LSD ($r = 0.197$, *p* value = 0.001). Moreover, SAD was correlated with cannabis ($r = 0.124$, *p* value = 0.035), opium ($r = 0.186$, *p* value = 0.001), methadone ($r = 0.152$, *p* value = 0.010), tramadol ($r = 0.258$, *p* value < 0.001), alcohol ($r = 0.133$, *p* value = 0.023), LSD ($r = 0.123$, *p* value = 0.036), and benzodiazepines ($r = 0.168$, *p* value = 0.004). The results indicated that none of the substances was correlated with GAD as well as agoraphobia (Table 4). However, agoraphobia had correlations with the intravenous injection as the main route of administration ($r = 0.174$, *p* value = 0.004).

The average duration of substance use was 15.86 years (SD = 10.04). The mean age of onset was 20.32 (SD = 7.53) for the substance use. Further analyses showed no correlations between anxiety disorders and other medical conditions (see "Procedure" section) such as viral infections, diabetes mellitus, thyroid disease, and coronary artery disease. Moreover, the duration of substance use and the age of onset were not correlated with any of the anxiety disorders (Tables 5 and 6).

Discussion

In this study, we aimed to identify the prevalence and probable associations of anxiety-related disorders with different substances used by patients diagnosed with substance use disorder.

Anxiety disorders (AD) and substance use disorder (SUD) are remarkably common, addressing the mental health and socio-economic conditions of individuals. Several reports have shown that co-occurrence of an AD and SUD affect the clinical course and treatment outcomes to a very great extent [19].

Concerning the main research question, it was found that there are probably anxiety-related symptom

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Table 1 Marital status, education level, and occupation of the subjects

	Marital status						Education level					Occupation			
	Single	Married	Widowed	Divorced	Separated	Missing	Illiterate	Did not finish high school	High school diploma	Bachelor's degree or higher	Missing	Employed	Unemployed	Retired	Missing
N	167	85	5	24	8	3	4	151	111	25	1	128	154	7	3
%	57.2	29.1	1.7	8.2	2.7	1.0	1.4	51.7	38.0	8.6	0.3	43.8	52.8	2.4	1.0

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Table 2 Frequency of different substances used by patients with substance use disorder

	Crystal	Cannabis	Opium	Heroin	Methadone	Tramadol	Alcohol	LSD	Benzodiazepine	Tobacco
N	157	130	140	145	127	82	123	44	111	261
%	53.8	44.5	47.9	49.7	43.5	28.1	42.1	15.1	38.0	89.4

Table 3 Frequency of different anxiety disorders in patients with substance use disorder

	PD[a]	Agoraphobia	SAD[b]	GAD[c]
N	31	17	64	83
%	10.6	5.8	21.9	28.4

[a] Panic disorder

[b] Social anxiety disorder

[c] Generalized anxiety disorder

patterns among patients with SUD. Moreover, the current study found that participants who were engaged in substance abuse were relatively young adults. In addition, a remarkable portion of the sample was at high risk of psychiatric problems regarding marital and socioeconomic status. Another important finding is that most of the participants were tobacco smokers (89.4%), but cigarette smoking was not correlated with any of the anxiety disorders. However, in a similar study by de Matos et al., tobacco dependence/abuse was

Table 4 Correlations between anxiety disorders and different substances used by patients with substance use disorder

		Crystal	Cannabis	Opium	Heroin	Methadone	Tramadol	Alcohol	LSD	Benzodiazepine	Tobacco
PD[a]	p value	0.900	0.047	0.667	0.081	0.563	0.000	0.058	0.001	0.744	0.875
	r	0.007	0.116	0.025	0.102	0.034	0.205	0.111	0.197	0.019	0.009
Agoraphobia	p value	0.658	0.425	0.682	0.207	0.771	0.503	0.550	0.320	0.580	0.913
	r	0.026	− 0.047	0.024	0.074	0.017	0.039	− 0.035	0.058	0.033	0.007
SAD[b]	p value	0.184	0.035	0.001	0.380	0.010	0.000	0.023	0.036	0.004	0.398
	r	0.078	0.124	0.186	0.052	0.152	0.258	0.133	0.123	0.168	− 0.051
GAD[c]	p value	0.516	0.423	0.072	0.229	0.954	0.057	0.810	0.213	0.710	0.786
	r	0.038	− 0.047	− 0.106	0.071	− 0.003	0.112	0.014	0.073	0.022	0.016

[a] Panic disorder

[b] Social anxiety disorder

[c] Generalized anxiety disorder

Table 5 Correlations between anxiety disorders and other medical conditions

		Diabetes mellitus N = 13	Thyroid disease N = 7	Coronary artery disease N = 10	Convulsion N = 20	HIV infection N = 2	HBV infection N = 2	HCV infection N = 4
PD[a]	p value	0.754	0.367	0.979	0.424	0.634	0.640	0.308
	r	− 0.019	− 0.054	− 0.002	− 0.048	− 0.024	− 0.028	0.062
Agoraphobia	p value	0.751	0.320	0.432	0.893	0.743	0.743	0.641
	r	0.019	0.059	− 0.047	− 0.008	− 0.020	− 0.020	-0.028
SAD[b]	p value	0.440	0.671	0.120	0.714	0.346	0.339	0.287
	r	0.046	0.025	0.093	0.022	0.057	0.058	− 0.065
GAD[c]	p value	0.149	0.990	0.552	0.452	0.491	0.485	0.899
	r	0.086	0.001	− 0.036	0.045	0.042	0.042	− 0.008

[a] Panic disorder

[b] Social anxiety disorder

[c] Generalized anxiety disorder

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Table 6 Correlations between anxiety disorders and the duration of substance use and the age of substance use onset

	Mean	Standard deviation	PD[a]		Agoraphobia		SAD[b]		GAD[c]	
			p value	*r*	*p* value	*r*	*p* value	*r*	*p* value	*r*
Duration (year)	15.86	10.04	0.951	− 0.004	0.560	0.037	0.992	0.001	0.478	− 0.080
Age of onset (year)	20.32	7.53	0.401	− 0.054	0.629	− 0.031	0.529	− 0.040	0.567	0.037

[a] Panic disorder

[b] Social anxiety disorder

[c] Generalized anxiety disorder

significantly prevalent in individuals with agoraphobia [6]. Another study by Ping Wu et al. on a sample of 781 adolescents revealed significant associations between cigarette smoking and AD in general among boys and girls. However, they found no evidence of associations between GAD and frequent cigarette smoking in males [32]. Crystal and heroin were the other two common substances reported by subjects. Although opium abuse was less common than heroin abuse in this study, other investigations in Iran have introduced opioid use disorder as the most common substance disorder [1]. However, this disagreement might be due to sample differences. As the participants of the current study were recruited from drug treatment services, the investigation by Amin-Esmaeili et al. was based on a household survey. Another possible explanation for this is that opium and opioids such as tramadol, methadone, etc. have been considered separately in this study. In addition, these findings might be indicative of a change in drug abuse patterns which needs to be addressed in future research with a wider scope. In this study, GAD was found to be the most common type of AD. This result reflects that of de Matos et al. who also reported that GAD is significantly prevalent in substance users. However, our research showed no significant correlations between a specific substance and GAD despite the high prevalence. In addition, the results indicate that cannabis, tramadol, and LSD are all associated with both PD and SAD. Regarding cannabis, different studies have shown diverse outcomes. Some studies reported that cannabis abuse was associated with SAD and GAD, but others showed no significant correlations [16]. In this study, no correlation was found between anxiety disorders and the duration of substance use regarding to their age of substance use onset. This might be due to the interruptions of substance use during their clinical course and then the distortion of the given information. In addition, none of the anxiety disorders were correlated to the other medical diseases. A possible explanation for this is the small number of the participants suffering from other medical conditions such as infections and coronary artery disease. Therefore, broader research with a larger sample size in each subgroup of the medical conditions is recommended.

A note of caution is due here since all the participants of this study were males. Gender differences might have considerable impacts on all the patterns discussed above. It is also important to bear in mind that all of the subjects were individuals seeking treatment or further assessments for simultaneous psychiatric disorders. These patients have probably higher insight of their health conditions due to disturbing symptoms, more severe problems, and medical advice on the reference to treatment centers which leads to higher presentation of comorbidities in the clinical setting. Therefore, these results need to be interpreted with caution as it may not be indicative of the trends in general population. The findings of this study support the notion that co-occurrence of psychiatric disorders is relatively common and must be taken into consideration when assessing a patient. Another limitation of this study was the missing and unreliable data on the dosage of substance used by the participants. The substance users often give imprecise information on the dosage. Moreover, due to the diversity of the sources of provision, the dosage cannot be relied on even in case of a good medical history.

The exact cause and effect patterns in AD and SUD are not well-established yet. This is probably due to the complexity of the biopsychosocial aspects of the psychiatric disorders. Difficulty in recalling the exact sequence of symptoms by the patients might be a problem when investigating the disorders to understand which one is the primary or the secondary cause. Many Studies have supported different causality pathways including "shared vulnerability", "precipitation", and "self-medication" hypotheses [8, 18]. Environmental factors such as family issues, lack of education, social stress, financial problems etc. can expose an individual to both AD and SUD. In addition, genetic susceptibility plays an important role as a common predisposing factor to psychiatric disorders. This idea which has been called the "shared vulnerability" hypothesis may explain the general correlations between SUD and AD regardless of the primary/secondary disorder. Additionally, the patients with SUD may

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experience subsequent anxiety-related symptoms due to the use and/or withdrawal of the illicit drugs. According to the "precipitation" model, these symptoms may finally lead to a secondary AD. Moreover, patients with anxiety-related symptoms may turn to illicit drugs to relieve their symptoms. This idea is explained by the "self-medication" hypothesis. For example, cannabis use may result in panic attacks and cessation of prolonged use of it may cause nervousness, sleep difficulties, restlessness, anxiety, and depressed mood. As a result, one may engage in more use of cannabis or other illicit drugs to overcome the disturbing symptoms of intoxication or withdrawal. Furthermore, patients with social anxiety disorder may use alcohol or cannabis to fit in the challenging social situations. Since this approach brings a relatively temporary relief and positive emotion, frequent drug abuse is likely to become problematic ending up in a vicious cycle. Although different mechanisms may underlie the co-occurrence of AD and SUD, it is beyond the scope of the current study to determine the ones that apply to this study group since the main focus of this study was to investigate the co-occurrence of the disorders. It should be pointed out that anxiety symptoms may be induced by the overdose or withdrawal of the substance. In the case of intoxication or withdrawal, the related symptoms are usually severe leading to the hospitalization of the substance users. Thus, these patients are usually managed in the inpatient rather than the outpatient settings.

Nonetheless, patients with AD are probably at higher risk of developing SUD and vice versa. Since comorbidities may complicate the treatment of SUD, this issue is important not only in the initial assessments but also in follow-up sessions. Thereby, an integrated and multidisciplinary approach is needed to understand which of these disorders should be targeted in different stages of treatment and rehabilitation. A future study with a larger sample size is recommended. Further work is required to explore the temporal precedence of AD and SUD and identify possible cause and effect mechanisms.

Conclusions

Patients with substance use disorder are potentially diagnosed with an anxiety disorder at the same time. Considering the frequent co-occurrence of these disorders and the correlations between a distinct substance and different anxiety disorders is of crucial importance when assessing patients and planning treatments and follow-ups.

Abbreviations
SCID-I: Structured Clinical Interview for DSM-V Axis I Disorders; DSM-V: Diagnostic and Statistical Manual of Mental Disorders 5th edition; AD: Anxiety disorder; SUD: Substance use disorder; PD: Panic disorder; GAD: Generalized anxiety disorder; SAD: Social anxiety disorder.

Authors' contributions
SS, MM, RS, and MAS: conceptualization and design of the study, methodology, data collection, supervision. AJN: investigation, data curation, original draft preparation, validation, formal analyses, visualization, reviewing, and editing manuscript. SN and MES: literature review, original draft preparation and validation. The author(s) read and approved the final manuscript.

Availability of data and materials
The dataset that was generated and analyzed during the current study will be made available on publication in an Open Science Framework repository on OSF.io.

Declarations

Consent to publication
Not applicable.

Ethics approval and consent to participate
Prior ethical approval was obtained from the Research Ethical Committee of Iran University of Medical Sciences to conduct this study (No. 15054). Permission was granted to use participants' data for current research by obtaining informed consent in Persian language based on the Declaration of Helsinki.

Competing interests
All authors declare that they have no competing interests.

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