

The impact of co-morbid alcohol use disorder in bipolar patients

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Abstract

Alcohol use is highly prevalent in patients with bipolar disorder (BD) and is associated with significant mortality and morbidity. The detrimental effects of each condition are compounded by the presence of the other. The objective of this study was to examine the impact of alcohol abuse and of alcohol dependence in BD in a Brazilian sample, as indicated by clinical severity, functional impairment, and quality of life (QOL). A cross-sectional survey of 186 bipolar outpatients were interviewed using the Structured Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders*—4th Edition. The primary outcome measures were functioning, as indicated by the Global Assessment of Functioning Scale scores and QOL, as indicated by the World Health Organization Quality of Life Instrument. Secondary outcomes were clinical severity features. Alcohol abuse and dependence were associated with male gender, lower education, earlier age of onset, psychosis within first episode, depressive symptoms, and worse functioning. In addition, the presence of alcohol abuse or dependence was associated with remarkably high rates of suicide attempt. Our findings suggest that the co-occurrence of alcohol abuse/dependence with BD increases the risk for suicide attempt, which may reflect in part the greater severity of symptoms and impaired functioning. This subgroup of bipolar patients requires a treatment tailored to address both conditions. © 2008 Elsevier Inc. All rights reserved.

Keywords: Bipolar disorder; Substance use disorder; Suicide; Functioning; Alcohol

Introduction

Alcohol use is highly prevalent in patients with bipolar disorder (BD) and is associated with significant mortality and morbidity (Mitchell et al., 2007). BD is the Axis I disorder associated with the highest risk for co-existing substance use disorder (SUD) (Weiss, 2004). In turn, a study reported that 60% of the subjects who presented with alcohol problems had undiagnosed BD (McKowen et al., 2005). The Epidemiological Catchment Area Study reported a 60.7% lifetime prevalence rate for substance abuse or dependence among those with type I BD, alcohol being the most common substance abused (Regier et al., 1990). More recently, the results from the National Epidemiological Survey on alcohol and related conditions have shown significant associations between mood and drug-use disorders, and suggest that co-morbid psychiatric disorders may increase the risk of greater involvement in more serious illicit

drug-use disorders (Conway et al., 2006). In clinical- and community-based samples, alcohol was also the most commonly abused substance (Brown et al., 2001; McElroy et al., 2001), and patients with type I BD had a 46% lifetime prevalence of alcohol-related disorders compared to only 14% in the general population (Brown et al., 2001). The co-occurrence of alcohol use disorders (AUD) and BD is associated with numerous negative consequences: greater risk of medication noncompliance, slower recovery from mood episodes, more frequent hospitalizations, suicides, and accidents (Goldstein & Levitt., 2008; Khalsa et al., 2008; Weiss, 2004).

BD on its own is associated with a high frequency of both suicide attempts and completed suicides, with 25–60% of patients making at least one suicide attempt during the course of their illness (Dalton et al., 2003). Likewise, alcohol consumption is a major risk factor for suicide (Nakaya et al., 2006; Sher, 2006; Sorock et al., 2006; Turecki, 2005). A prospective cohort study conducted in Japanese men indicated a significant positive association between the daily amount of alcohol consumption and suicide risk (Nakaya et al., 2006). A *Diagnostic and Statistical Manual of Mental Disorders*—4th Edition (DSM-IV)

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AXIS I diagnosis is present in about 90% of those who commit suicide (Turecki, 2005), which seems to be the cause of death in 5–15% of BD patients (Dalton et al., 2003). According to Valtonen et al. (Valtonen et al., 2006), during a medium-term follow-up, as many as one fifth of random psychiatric patients with BD attempted suicide, which highlights the public health importance of suicidal behavior in BD. Previous suicide attempts, hopelessness, and depressive phase were the key indicators of the risk (Valtonen et al., 2006). Also, SUDs rank second only to mood disorders as a risk factor for suicide attempts (Dalton et al., 2003). Patients with BD are likely to have a co-morbid diagnosis of SUD and this co-morbidity pattern appears to increase the risk of a suicide attempt up to twofold (Dalton et al., 2003). Alcohol dependence is an important risk factor for suicidal behavior, and lifetime mortality due to suicide in alcohol dependence has been reported to be as high as 18% (Sher, 2006). Individuals with alcohol dependence have a 60–120 times greater suicide risk than the nonpsychiatric population (Sher, 2006). Moreover, suicide attempters and completers have a more severe form of alcoholism compared to individuals with alcoholism who never attempted suicide (Sher, 2006).

One fact underlying the association between SUD and suicide attempts may be the severity of illness: subjects with a more severe form of BD may be more likely to both attempt suicide and use substances as self-medications (Dalton et al., 2003). In addition, the coexistence of BD and AUD may synergistically contribute to impairments in functioning and quality of life (QOL), including poorer social support, a known risk factor for suicide. A history of alcohol abuse or dependence has been reported to lead to lower QOL ratings in patients with BD (Singh et al., 2005). Similarly, anxiety could be another risk factor for suicide, which is associated with both BD and AUD (Simon et al., 2004). High rates of AUD have been associated with high prevalence of anxiety disorders in those with BD (Goldstein & Levitt, 2008), consistent with the anxiolytic effects of alcohol. For instance, a study of the first 500 patients enrolled in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) found that BD patients with lifetime anxiety disorders had roughly double the prevalence of lifetime alcohol dependence and a 50% greater prevalence of lifetime drug dependence compared to BD patients without lifetime anxiety disorders (Simon et al., 2004).

The detrimental effects of each disorder are compounded by the presence of the other (Mitchell et al., *in press*), and patients are more likely to relapse following treatment of their SUD if they have a co-morbid psychiatric disorder. In turn, concurrent SUD increases the chronicity, disability, and mortality rates associated with BD (Mitchell et al., *in press*). Accordingly, numerous case reports and surveys indicate that the use of relatively small amounts of alcohol and other drugs by those with severe mental illness adversely affects their psychiatric stability (exacerbation of illness) and psychosocial adjustment (problems of

behavior, relationships, finances, and housing) (Drake & Mueser, 2000).

Despite the greater prevalence, unique pharmacological effects, and wide availability of alcohol compared to other illicit drugs of abuse, for diverse reasons, a number of previous studies in BD have combined alcohol and other substances' use disorders. In addition, many studies combine abuse and dependence in the same category, and only more recently have the different patterns of alcohol consumption in BD been examined (Goldstein et al., 2006; McKowen et al., 2005). The findings suggest that even a moderate amount of alcohol consumption could have deleterious effect in BD (Goldstein et al., 2006), and individuals with alcohol abuse, although not alcohol dependent, may have repeated legal, interpersonal, social, or occupational impairments related to alcohol consumption, frequently using alcohol in physically hazardous situations (Sher, 2006). These data are relevant to reinforce preventive strategies in clinical settings. Patients commonly give low importance to alcohol abuse, but this may be a particularly dangerous assumption in BD patients, a known vulnerable population. In fact, Castaneda et al. (1996) reviewed the potential theoretical mechanisms by which moderate alcohol use could exacerbate mood disorders, and concluded that abstinence from alcohol should be recommended for those patients.

Although this subject has been a matter of study in other countries for some decades, in South America, and specifically in Brazil, we have no knowledge of reports on the associations between BD and AUD, and of its clinical and psychosocial impact. Given the previously reported high prevalence and deleterious impact of alcohol use in the course of BD, the objective of this study was to examine the impact of alcohol abuse and of alcohol dependence in BD in a Brazilian sample; we hypothesized that BD patients who do not use alcohol would present with a better clinical course and/or outcome, associated with better functioning and QOL, and that BD patients with alcohol abuse, and those with alcohol dependence would present with worse clinical parameters, as well as lower functioning and lower self-reported QOL.

Methods

One hundred eighty-six outpatients with BD type I or II were consecutively recruited from the Bipolar Disorders Program of the University Hospital at the Federal University, Porto Alegre, Brazil, from September 2003 to June 2007. The diagnosis was confirmed with the Structured Clinical Interview for DSM-IV-AXIS I (SCID I). We also used a previously described standard protocol (Gazalle et al., 2005) for collection of sociodemographic and clinical variables. The number of lifetime suicide attempts was assessed as part of this protocol. Lifetime AUD (alcohol abuse/dependence) was defined according to DSM-IV and confirmed with the SCID I. The subgroup "alcohol abuse" included abuse only, whereas the "alcohol dependence"

group included patients with alcohol dependence with or without abuse. Anxiety disorder co-morbidity categories included panic disorder, post-traumatic stress disorder, obsessive-compulsive disorder, general anxiety disorder, social phobia, and phobia, whereas any drug co-morbidity included cocaine, tetrahydrocannabinol (THC), stimulants, opioids, and nicotine (cigarettes) abuse and/or dependence; these were assessed through the SCID I. QOL was assessed using the World Health Organization Quality of Life Assessment—Abbreviated version (WHOQOL-BREF) (WHO-QOL Group, 1998).

Written informed consent was obtained from all patients before study entry. This research project received approval from the local ethics committee.

Statistical analysis

Descriptive statistics were used to report sociodemographic and clinical characteristics of the sample. For analysis purposes, the sample was divided into three groups: (1) patients without alcohol co-morbidity ($N = 125$); (2) patients with alcohol abuse ($N = 23$); and (3) patients with alcohol dependence ($N = 30$). The association between dichotomous variables was assessed with χ^2 test or Fisher's exact test as appropriate, and logistic regression was used to control the analyses to gender. Differences between groups regarding all other sociodemographic characteristics and clinical features were evaluated through analysis of variance (ANOVA) test and Tukey post hoc test when appropriate. These were exploratory analyses as the sample size restricted the power to detect smaller effect sizes and precluded meaningful stratifications. All statistical tests were two-tailed and were carried out using a significance level of $\alpha = 0.05$. Data are presented as means \pm standard deviation. Statistical analyses were performed using the Statistical Package for Social Sciences version 13.0 (SPSS Inc., Chicago, IL, USA).

Results

Of the 186 recruited patients, 54 (29%) were male and 132 (71%) were female. There was a significant difference between the three groups regarding gender and education (Table 1); patients with AUD being more likely to be males and to have lower education. Mean age and ethnicity did not differ significantly between the three groups.

Clinical variables indicated that patients with alcohol abuse/dependence were more likely to present earlier illness onset, and to display psychotic symptoms during the first episode (Table 1); they also showed more depressive symptoms and poorer functioning, as indicated by higher Hamilton Depression Rating Scale (HAM-D) scores and lower scores on the Global Assessment of Functioning (GAF) Scale (Table 1). We did not find significant differences between the three groups regarding illness duration, number of psychiatric hospitalizations, and Young Mania Rating Scale (YMRS) scores (Table 1).

There were no statistically significant differences in self-reported QOL measures for the alcohol abuse group in relation to those without the condition: physical domain ($t = 0.232$; degree of freedom [df] = 143; $P = .452$); psychological domain ($t = 0.805$; $df = 143$; $P = .463$); social domain ($t = 0.716$; $df = 143$; $P = .244$); and environmental domain ($t = 0.567$; $df = 143$; $P = .386$). Similarly, the "alcohol dependence" group did not show statistically significant differences from those without the condition regarding QOL scores: physical domain ($t = 0.616$; $df = 143$; $P = .221$); psychological domain ($t = 0.852$; $df = 143$; $P = .316$); social domain ($t = 1.471$; $df = 143$; $P = .626$); and environmental domain ($t = 0.319$; $df = 143$; $P = .319$).

Regarding co-morbidities, there were no statistically significant differences between the three groups regarding the prevalence of any anxiety disorder. As expected, there was a significant association between alcohol abuse and dependence, and abuse and dependence of other, namely cocaine, THC, stimulants, opioids, and nicotine (cigarettes), as shown on Table 2.

For the whole sample, the lifetime suicide attempts prevalence was 51.1%. Alcohol abuse was associated with markedly higher rates of suicide attempts compared to BD patients without that co-morbidity (Fig. 1). In our sample of BD outpatients, we found that, for both the comorbid abuse and the dependence groups, there was a higher percentage of consumers in the group of lifetime suicide attempters than in the group of nonattempters: (1) 65.3% of alcohol-abuse patients in the group of attempters, and 34.7% in the group of nonattempters ($\chi^2 = 5.392$; $df = 1$; $P = .015$); and (2) 67.7% of alcohol-dependent patients in the group of attempters, and 32.3% in the group of nonattempters ($\chi^2 = 4.135$; $df = 1$; $P = .032$).

To further investigate the association between alcohol abuse/dependence and suicide attempts, we examined the association with consumption of other drugs. The analysis was stratified into four groups: (1) *no alcohol or drugs*, showing a 49.5% lifetime rate of suicide attempts and a 71.4% rate of no lifetime suicide attempts; (2) *alcohol consumption*, in which 21.1% patients presented a lifetime suicide attempt history and 8.8% no history; (3) *drugs*, 12.6% of patients presenting a suicide attempt history and 9.9% without that history; and (4) *alcohol and drugs*, in which 16.8% patients presented a lifetime suicide attempt history and 9.9% did not present that history ($\chi^2 = 10.343$; $df = 3$; $P = .016$).

Differences in *lifetime* number of suicide attempts between the SUD groups (no alcohol co-morbidity, alcohol abuse, alcohol dependence) were analyzed with ANOVA ($F = 2.898$; $df = 3$; $P = .038$).

Discussion

The results showed that alcohol abuse or dependence were associated with male gender, lower education, earlier

Table 1
Sociodemographic and clinical features

Variables	BD patients with no alcohol comorbidity (N = 125)		BD patients with alcohol abuse (N = 23)		BD patients with alcohol dependence (N = 30)		ANOVA		
	Mean	S.D.	Mean	S.D.	Mean	S.D.	χ^2	P value	Tukey post hoc test*
Gender (% male)	21.4		34.8		58.1		13.495	.001	
Ethnicity (% Caucasian)	82.5		91.3		83.9		1.102	.575	
Psychosis in first episode (%)	47.6		56.5		33.3		2.722	.02	
Age (years)	43.9	11.92	37.7	9.51	42.1	9.40	3.016	.068	0.043/0.709
Education (years)	9.2	4.07	11.8	3.89	9.1	4.29	4.056	.045	0.017/0.044
Age of illness onset	27.7	11.92	19.2	7.76	21.9	11.85	7.049	.003	0.004/0.041
Illness duration	16.3	11.47	18.4	11.73	19.7	10.95	1.192	.442	0.697/0.325
Number of hospitalizations	3.6	4.65	4.6	4.95	3.8	4.54	0.436	.474	0.628/0.989
YMRS	4.4	5.64	5.3	5.45	5.9	6.70	0.936	.486	0.787/0.399
HAM-D	8.8	7.21	10.9	6.66	12.7	7.65	4.098	.018	0.395/0.019
GAF	65.5	15.07	52.7	7.25	60.9	11.73	3.342	.038	0.512/0.036

BD = bipolar disorder; ANOVA = analysis of variance; S.D. = standard deviation.

*Between groups.

age of BD onset, psychosis during the first episode, more depressive symptoms, and worse psychosocial functioning. In addition, the presence of alcohol abuse or dependence was associated with high rates of suicide attempts.

Regarding sociodemographic aspects, our results are in agreement with those reported by Frye and Salloum (2006), who found a significantly greater prevalence of *lifetime* alcohol co-morbidity in men. Likewise, our results suggest that men are more likely to be in the *co-morbidity* group than in the *non-co-morbidity* group, whereas for women the opposite occurs. It is important to mention that, although women with BD had a lower prevalence of *lifetime* alcoholism compared to men, there is evidence that they are particularly vulnerable to alcohol dependence, compared to the general female population (odds

ratio = 7.35) (Frye et al., 2003). The findings of a statistically significant difference in education ($P = .045$), in line with recent data (Weiss et al., 2005), show that patients with past history or current SUD are less likely to have college education compared to patients with no SUD. We found no statistically significant differences in both the mean age and in ethnicity between groups. The sample included only patients who were referred to the public health system due to severe and persistent mental illness, and the majority were Caucasian.

As shown in Table 1, patients with alcohol abuse or dependence showed an earlier illness onset than those without the condition, which is in line with previous findings (Winokur et al., 1996). Winokur et al. (1995) suggested that the early onset group had a more severe bipolar illness that

Table 2
Comorbidities: anxiety disorders and substance abuse disorder (SUD)

Variable	BD patients with no alcohol comorbidity (N = 125) (%)	BD patients with alcohol abuse (N = 23) (%)	Odds ratio (CI 95%)	P value*	BD patients with alcohol dependence (N = 30) (%)	Odds ratio (CI 95%)	P value*
Any anxiety disorder	40.50	52.20	0.440 (0.195–0.994)	.048	58.10	0.715 (0.237–2.159)	.552
PD	12.70	12.00	0.606 (0.216–1.704)	.340	19.40	0.625 (0.139–2.816)	.541
PTSD	13.50	21.70	0.448 (0.173–1.163)	.099	25.80	0.779 (0.223–2.862)	.730
OCD	11.10	13.00	0.429 (0.156–1.175)	.100	22.60	0.514 (0.117–2.252)	.378
GAD	9.50	17.40	0.439 (0.150–1.280)	.439	19.40	0.877 (0.217–3.553)	.132
Social phobia	15.90	34.80	0.981 (0.337–2.862)	.972	16.10	2.793 (0.760–10.912)	.120
Phobia	19.00	17.40	0.953 (0.294–3.088)	.937	16.10	0.980 (0.322–2.912)	.972
Any drug abuse/dependence	15.10	43.50	0.178 (0.075–0.421)	<.001	48.40	0.161 (0.092–0.736)	.001
Cocaine	4.80	26.10	0.353 (0.107–1.165)	.087	16.10	1.444 (0.364–5.728)	.601
THC	7.10	34.80	0.264 (0.089–0.777)	.016	22.40	1.823 (0.561–5.922)	.318
Stimulants	4.00	26.10	0.143 (0.042–0.488)	.002	22.60	1.210 (0.345–4.245)	.766
Opioids	0.80	8.70	0.042 (0.005–0.371)	.042	9.70	0.780 (0.166–3.658)	.780
Nicotine (cigarettes)	23.00	40.90	0.999 (0.312–2.980)	.085	41.90	0.967 (0.412–2.742)	.090

BD = bipolar disorder; PD = panic disorder; PTSD = posttraumatic stress disorder; OCD = obsessive-compulsive disorder; GAD = general anxiety disorder; THC = tetrahydrocannabinol.

*Logistic regression adjusted to gender.

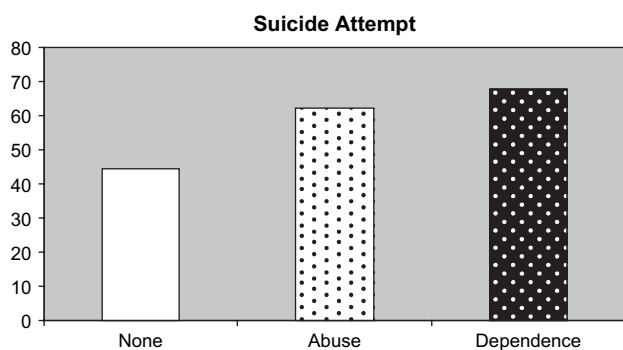


Fig. 1. Prevalence of patients with bipolar disorder and a previous suicide attempt among those with or without alcohol abuse/dependence.

included the development of alcohol consumption, whereas patients with prior alcohol consumption had a less severe illness that required the presence of alcoholism for the manifestation of BD. Winokur et al. (1998) defined patients in whom BD symptoms began prior to the onset of alcohol consumption as “primary bipolar disorder” and the converse as “primary alcoholism,” this distinction predicting different courses of BD. Another clinical feature associated with AUD in our sample was psychosis in the first episode. Tsai et al. (2002) showed that mood-incongruent psychotic features predict poor outcome in BD, and that a person who is psychotic during the first episode of an affective illness is very likely to become psychotic during subsequent episodes. Moreover, alcohol consumption in BD has been associated with mixed affective states (Strakowski et al., 2005), this association being clinically relevant because these states tend to be more difficult to treat than pure manic or depressive episodes and may represent a more severe type of mood episode (Strakowski et al., 2005), including psychotic features (Pini et al., 2004). The present study did not intend to determine whether BD manifested before AUD or vice versa; nevertheless, it would be interesting to assess if those patients with psychotic symptoms in the first episode are the patients in whom BD manifested first. Winokur et al. (1995, 1998) suggested that the former group of patients would present a more severe course of bipolar illness (Strakowski et al., 2005), with an earlier age of onset and a worse course of BD (Cassano et al., 2000).

As referred by Weiss et al. (2005), a lifetime history of SUD (past or current) in BD patients is associated with worse outcomes. In agreement with data from the National Comorbidity Survey, which demonstrated a twofold increase in the lifetime odds of depression among subjects with alcohol dependence our results showed that alcohol abuse and dependence are associated also with depressive symptoms. Notably, major depressive episodes greatly increase the risk for attempted and completed suicide (Sher, 2006). Moreover, an increase in severity of depressive symptoms has been reported in those with AUD co-morbidity (Frye et al., 2006).

Patients with co-occurring BD and SUD are prone to adverse consequences, including a variety of psychosocial

difficulties, such as legal problems, unemployment, and homelessness (Drake et al., 2004). These are likely to affect functioning, which is confirmed by our findings of lower scores in the GAF for those with co-morbidity than for those without. The co-occurrence of SUD and BD increases chronicity, disability, and mortality. Surprisingly, we did not find significant differences between the groups in any of the four domains of the WHOQOL-BREF, which is not consistent with other reports (Singh et al., 2005), in which patients with AUD and BD self-reported lower QOL on all domains as compared to those without the condition. Also, the same authors suggested that dual-diagnosis patients experienced a poorer QOL compared to patients with either BD or SUD alone. Therefore, in our sample, BD and AUD co-morbidity were associated with discrepancies between GAF scores and self-reported QOL; this could be related to the lack of insight in these patients. Indeed, the self-evaluation character of QOL can be at the same time the strength and the weakness of this kind of assessment. Patients with co-occurrent BD and alcohol abuse have particularly high rates of cognitive impairment, denial, and poor insight (Mitchell, in press), making it difficult for them to adequately self-evaluate their own illness condition and associated hazards, which may lead to persistence or even a worsening of the alcohol consumption pattern. These aspects should be taken into account when examining and dealing with this special population.

It has been previously reported (Chen & Dilsaver, 1996) that 25–60% of bipolar patients make at least one suicide attempt during the course of their illness. Our findings in a Brazilian sample, revealed a lifetime prevalence of suicide attempts of 51.1% in those with BD. Those with AUD are more likely to be in the group of lifetime suicide attempters than in the group of nonattempters. There is a trend line indicating that the more severe the alcohol co-morbidity, the higher the number of suicide attempts. Our findings are in line with a prospective cohort study conducted in Japanese men, which indicated a statistically significant positive linear association between the daily amount of alcohol consumption and the risk of suicide (Nakaya et al., 2006); this study found that the risk of suicide was significantly increased among heavy drinkers, defined as (≥ 45.6 g of alcohol per day), as compared to that of non-drinkers (Nakaya et al., 2006). Similarly, we found a statistically significant difference in suicide attempts between groups—no alcohol co-morbidity, abuse only, and dependence; this could indicate that the deleterious effect of alcohol on suicide attempts may occur regardless the pattern of use, as it would be the substance itself responsible for the effects on suicide attempts outcome on BD patients.

Considering the concomitant consumption of other drugs, either alone or along with alcohol by bipolar patients, it is worthy to say that for the group 1 *without alcohol or drugs* only, we found a higher percentage of *no lifetime suicide attempts*; for groups 2, 3, and 4 (either alcohol or drug consumption alone or alcohol and drug

consumption), we found a higher percentage of lifetime suicide attempters than nonattempters. Regarding the association between drug use and suicide attempts, our results are partially in line with Dalton et al. (2003), who showed a significant association between SUD (only drug abuse and dependence, but no alcohol abuse and dependence) and increased risk of lifetime suicide attempts; in our sample, we found an association for both alcohol and drugs regarding lifetime suicide attempts.

It is important to mention that SUD manifest differently in people with severe mental illnesses, the central difference being that individuals with severe mental illnesses have a heightened sensitivity to the effects of psychoactive substances (Drake & Mueser, 2000).

Regarding BD specifically, it remains unclear whether SUDs are more prevalent in a subgroup of patients with a more severe disease process or whether SUDs themselves have a deleterious impact on BD course. It is likely that part of the severity of the course in patients with current or past SUD is due to both effects of the SUD itself and the severity of the co-occurring BD (Weiss et al., 2005). A plausible hypothesis for the worsening in the course of BD relies on the allostatic load concept (Kapczinski et al., 2008); these authors postulate that psychiatric co-morbidities, and especially SUD, would be equivalent to repeated stress with neurotoxic consequences, increasing the deleterious effects of allostasis, which in turn may worsen the disease process of BD. This phenomenon would engender worse BD outcomes, higher rates of suicide attempts, longer time to achieve remission, and higher risk for relapse, with each episode functioning itself as a repeated stress, with its own impact in allostatic load (Kapczinski et al., 2008). In turn, the continuity of consumption may contribute to the even more hazardous impact of the co-morbidity on the outcomes of BD, considering the previously mentioned impact of substance use on allostatic load (Kapczinski et al., 2008).

Our results should be interpreted taking some limitations under consideration. The sample size is relatively small; possibly a reflection of the reluctance of these dual-diagnosed patients to look for treatment and to be recruited. Furthermore, we did not evaluate cognition and insight, which may have biased QOL results. Moreover, patients were heterogeneous in symptom intensity, and this could have also influenced the results concerning psychosocial functioning and QOL. Finally, taking into account the cross-sectional design of the study, the conclusions should be limited to associations but not causality.

Bearing these limitations in mind, our study is the first South American study to report on this topic, and was able to replicate the findings of previous groups in other parts of the world. The present results reinforce the importance of identifying these patients with co-morbidity as a special population, pointing to the fact that they should be diagnosed early and managed for AUD whatever the pattern of use (abuse or dependence) is, because both patterns seem to be hazardous to the course of BD.

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