

Anxiety Comorbidity and Quality of Life in Bipolar Disorder Patients

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Objective: To assess the impact of anxiety comorbidity on the quality of life of patients with bipolar disorder (BD).

Methods: We undertook a cross-Sectional survey of 162 BD outpatients interviewed with the Structured Clinical Interview for DSM-IV. The primary outcome measure was quality of life, assessed with the 26-item WHO Quality of Life Instrument (WHOQOL-BREF).

Results: Anxiety comorbidity in BD patients was associated with lower scores in all domains of quality of life. The impact of anxiety comorbidity on the psychological domain of the WHOQOL-BREF was kept, even when the current level of depression was added to the model as a confounding factor. Current anxiety comorbidity was also associated with lifetime alcohol abuse and dependence, rapid cycling, lifetime psychosis, number of suicide attempts, and a lower score in the Global Assessment of Functioning measure.

Conclusion: Our findings suggest that anxiety comorbidity in BD patients is related to lower quality of life, particularly on the psychological domain. BD–anxiety comorbidity may be associated with such markers of illness severity as number of suicide attempts, rapid cycling, lifetime alcohol abuse, and psychosis. The recognition and treatment of anxiety comorbidity may help patients with BD to relieve their psychological pain and improve their overall quality of life.

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Clinical Implications

- Anxiety comorbidity is highly prevalent among BD patients, with a great impact on quality of life, and warrants routine clinical assessment and better specific management.
- The comprehension of a relation between BD–anxiety comorbidity and quality of life suggests the importance of routine screening for other associated factors, such as suicide risk, rapid cycling, and alcohol abuse.
- Quality of life has increasingly become an outcome measure for treatment trials. Multiple factors, such as anxiety comorbidity, may affect quality of life and can be more specifically targeted in treatment interventions.

Limitations

- This study had a cross-Sectional design, so no causative evidence could be taken.
- The anxiety disorders have been combined here, although they are not all alike.
- Investigation of a broad concept such as quality of life may be affected by other possible confounders not considered here.

Key Words: bipolar disorder, quality of life, anxiety, comorbidity

The clinical presentation of BD is usually associated with psychological suffering, functional impairment, interpersonal problems, and a substantial economic burden.^{1,2} An emerging body of evidence shows that BD is associated with lower scores on quality of life.³⁻⁶ Quality of life seems to be impaired during mood episodes⁷ and in the presence of subsyndromal symptoms,⁸ but not in euthymic patients.⁹ BD patients with higher scores for depression were reported to present lower scores for quality of life.^{3,10} There is evidence that patients with bipolar depression present lower quality of life than unipolar patients,³ but the level of depression does not seem to fully explain the lower quality of life among patients with BD.^{10,11} Anxiety is a frequent complaint among patients with BD,¹² and anxious comorbidities are more prevalent among patients with BD than among patients with unipolar depression.^{13,14} There is also evidence that generalized anxiety disorder, OCD, social phobia, and PTSD are associated with lower quality of life.^{15,16} Therefore, the subjective experience of being anxious could be a concurrent factor for the determination of lower quality of life among patients with BD.

Epidemiologic studies have demonstrated that individuals with BD have higher rates of comorbid anxiety disorders than are found in the general population.^{17,18} In the National Comorbidity Survey, 92.9% of the subjects who met criteria for lifetime BD I also met criteria for any lifetime anxiety disorder, compared with 24.9% of the general population sample.^{18,19} Data from the Epidemiological Catchment Area Study showed that 21% of BD I and II patients had lifetime panic disorder and 21% had lifetime OCD.¹⁹ Recent studies suggest that BD with comorbid anxiety may be associated with greater illness severity and poorer outcomes.^{4,20,21} BD patients with comorbid anxiety have been described as more

likely to present suicidal behaviour, substance abuse, more severe side effects from medication, and a longer time to achieve remission.²⁰⁻²² Frequently, more than one anxiety disorder is encountered in BD subjects,^{23,24} which might be another factor affecting the prognosis. Thus BD comorbid with anxiety might lead to prominent problems in social relationships, employment, psychopathology, and global functioning in the long term. The magnitude of the impact of such impairments can be difficult to assess. For this purpose, quality-of-life measures may be an interesting tool. Most quality of life instruments assess different domains, such as the physical, psychic, environmental, and social. Quality of life as defined by the WHO is a broad concept that considers

the individual's perception of his or her position in life, within the cultural context and value system he or she lives in, and in relation to his or her goals, expectations, parameters, and social relations.^{25, p1570}

Intriguingly, few studies to date examine the impact of anxiety comorbidity on the quality of life of individuals with BD. One recent study reported decreased quality of life in BD patients with anxiety comorbidity, compared with patients not suffering from anxiety comorbidity.²⁶ Therefore, the present study aims to evaluate whether BD patients with comorbid anxiety have lower quality of life and a more severe clinical presentation.

Methods

This study was a cross-sectional survey of 162 outpatients with BD, aged 18 years or older, consecutively recruited from the Bipolar Disorders Program of the University Hospital at the Federal University, Porto Alegre, Brazil, between 1 September 2003 and 15 January 2005. The subjects received a diagnosis based on the SCID-I.²⁷ We included patients with BD I and II at different stages of recovery. All patients gave written informed consent before entering into the study. The study was approved by the local ethics committee. We divided our sample into 2 major groups: patients with ($n = 91$) and without ($n = 71$) current comorbid anxiety disorder (that is, panic disorder with or without agoraphobia, agoraphobia without panic disorder, OCD, generalized anxiety disorder, social phobia, specific phobia, PTSD, and anxiety disorder not otherwise specified).

Quality of life was considered our primary outcome measure, and we assessed it with the 26-item WHOQOL-BREF,²⁸ a multidimensional, self-administered scale that covers 4 quality-of-life domains (psychological, environmental, social relationships, and physical health). Items are rated on a 5-point scale in which 1 indicates low, negative perceptions and 5 indicates high, positive perceptions. The instrument was previously validated in a Brazilian sample. The validation of the Portuguese version of the WHOQOL-BREF showed high

Abbreviations used in this article

ANOVA	analysis of variance
BD	bipolar disorder
CI	confidence interval
GAF	Global Assessment of Functioning
HDRS	Hamilton Depression Rating Scale
OCD	obsessive-compulsive disorder
PTSD	posttraumatic stress disorder
SCID-I	Structured Clinical Interview for DSM-IV Axis I
SD	standard deviation
WHOQOL-BREF	World Health Organization Quality of Life Instrument

Table 1 Sociodemographic variables among patients with BD

Variable	BD patients		P
	Anxiety (n = 91)	No anxiety (n = 71)	
Sex			0.60 ^a
Men, %	38.0	28.1	
Women, %	62.0	71.9	
Age, years			
Mean (SD)	43.1 (11.0)	42.0 (11.8)	0.52 ^b
< 40, %	38.0	41.8	0.88 ^a
40–59, %	57.7	53.8	
≥ 60, %	4.2	4.4	

^aChi-square test; ^bt test

rates of reliability, internal consistency, and construct validity.²⁸

Assessments of demographic status and clinical psychopathological features were performed with a previously used, semistructured questionnaire.¹⁰ We assessed substance abuse or dependence, rapid cycling, and lifetime psychosis according to DSM-IV criteria. We assessed global functioning with the GAF measure and depressive symptoms with HDRS.²⁹

Statistical Analysis

The 4 WHOQOL-BREF domains (physical, psychological, social, and environmental) were analyzed separately. Descriptive analyses included calculation of proportions and respective 95% CIs for categorical variables. We calculated means, medians, SDs, and percentiles for continuous variables, and we used histograms and the Kolmogorov–Smirnov test to check variables for normality. The chi-square tests for heterogeneity were used to test differences in proportions. We applied the nonparametrical Kruskal–Wallis test to compare medians and the *t* test and ANOVA for heterogeneity to compare means. We used chi-square tests for heterogeneity for dichotomous outcomes such as substance abuse or dependence, rapid cycling, and psychosis. Continuous outcomes (age at onset, suicide attempts, and hospitalizations) were analyzed with ANOVA. Sex, age, family income, and level of depression were controlled with a linear regression model.

Results

There were no statistical differences between anxious BD patients and the nonanxious BD subgroup in relation to sociodemographic variables (Table 1). The prevalence of overall current anxiety comorbidity in this sample was 56.1%.

The most frequent anxiety disorder was specific phobia (32.1%), followed by agoraphobia (17.9%), social phobia (14.8%), generalized anxiety disorder (11.7%), and panic disorder (11.1%). The prevalence of OCD was 10.6%, and the prevalence of PTSD was 10.5%.

Crude analysis showed that anxious BD patients had lower scores in all WHOQOL-BREF domains (Wald test, $P < 0.05$; see Table 2). After adjusting for age, sex, and family income, a significant impairment persisted in the psychological ($P = 0.031$) and social ($P < 0.001$) WHOQOL-BREF domains but not in the physical ($P = 0.300$) and environmental ($P = 0.062$) domains. However, after we added the level of depressive symptoms (according to the HDRS) as a confounder, only the psychological domain of the WHOQOL-BREF showed significant impairment (Wald test, $P = 0.002$), suggesting that comorbid anxiety may influence the quality of life of BD patients, regardless of the presence of depression.

Anxious BD patients had higher rates of suicide attempts (ANOVA, $P = 0.007$) than did nonanxious BD patients (Table 3). Anxious BD patients were more likely to present lifetime alcohol abuse and dependence (chi-square test, $P = 0.04$), rapid cycling (chi-square test, $P = 0.027$), and lifetime psychosis (chi-square test, $P = 0.021$). The group with anxiety comorbidity showed lower GAF scores (ANOVA, $P = 0.018$). Conversely, we found no between-group differences in lifetime drug abuse or dependence, number of hospitalizations, and age at onset ($P > 0.05$).

Discussion

The present study showed that BD patients with current comorbid anxiety present lower quality-of-life scores. The effect of anxiety on the psychological domain of quality of life

Table 2 Quality of life among BD patients with and without current anxiety comorbidity

WHOQOL domains	Crude analysis		Adjusted analysis ^a	
	Coefficient (95%CI)	P ^b	Coefficient (95%CI)	P ^b
Physical				
Anxiety	Reference	0.001	Reference	0.072
No anxiety	-0.3 (-17.2 to -4.7)		-0.1 (-10.8 to 0.5)	
Psychological				
Anxiety	Reference	0.001	Reference	0.001
No anxiety	-0.4 (-21.2 to -9.3)		-0.2 (-14.2 to -3.9)	
Social				
Anxiety	Reference	0.001	Reference	0.089
No anxiety	-0.2 (-18.6 to -4.6)		-0.1 (-12.3 to 0.9)	
Environmental				
Anxiety	Reference	0.005	Reference	0.179
No anxiety	-0.2 (-14.7 to -2.1)		-0.1 (-8.1 to 1.5)	

^aAdjusted for HDRS
^bWald test

is kept, even when the level of depression is controlled for. This finding supports the notion that anxious comorbidity has a negative impact on quality of life in patients with BD, regardless of the presence of depression. Previous studies have shown that quality of life is inversely correlated with the level of depression. The magnitude of such correlation was reported to be in the order of -0.1 to -0.3³ and up to -0.3 to -0.6.¹¹ According to these figures, one can argue that the correlation between depression and quality of life may be consistent but is far from being the sole explanation for the impaired quality of life found in patients with BD. Indeed, patients with bipolar depression are likely to present poorer quality of life than patients with unipolar depression,^{3,11} even when the level of depression is matched between groups.¹¹ Our study suggests that the variance in quality of life among BD patients can be explained, at least in part, by anxiety comorbidity.

We also found that patients with comorbid BD and anxiety present more severe psychopathological features, namely, higher rates of alcohol abuse or dependence, lifetime psychosis, suicide attempts, and rapid cycling, as well as lower GAF scores. These findings accord with previous studies that found higher rates of alcohol abuse or dependence, elevated risk of suicide attempts, and impaired functioning in subjects with comorbid BD and anxiety.^{4,21,30} Cassano et al³¹ found an increased prevalence of panic disorder, OCD, and social phobia in subjects with affective psychosis, who were mostly BD I patients. Further, they observed that patients with multiple anxiety disorders had more severe psychopathology and

substance abuse.³¹ A recent prospective study confirmed data showing greater severity and lower quality of life in BD patients with anxiety comorbidity, compared with patients without anxiety comorbidity after 1 year of follow-up.²⁶ Interestingly, the association between anxiety-BD comorbidity and rapid cycling is poorly discussed in the literature.³² In a recent multisite study with a large sample of BD patients, MacKinnon et al³³ reported that rapid mood switching was associated with a higher risk of presenting anxiety disorders and substance abuse. Taken together, these findings show that comorbid anxiety may negatively influence the course of BD.

Although previous studies have reported an earlier age of onset, a higher prevalence of lifetime drug abuse or dependence, and a higher number of hospitalizations in subjects with comorbid BD and anxiety, we did not find such association. This discrepancy may be associated with different assessment methods and sample characteristics. We collected age-of-onset data retrospectively, so a recall bias should be considered. Further, we studied an exclusively outpatient sample of BD patients from an academic specialty centre in Brazil.

Qualitative differences between the subjective experience of suffering from unipolar and bipolar depression are difficult to grasp. Differential clinical features, such as a higher risk of suicide among BD patients, suggest that bipolar and unipolar depression are not necessarily closely related. Early psychopathological descriptions highlighted the distinctive nature of the “inner turmoil” and incapacitation presented by

Table 3 Clinical features of BD patients with and without current anxiety comorbidity

Clinical feature	BD patients		P
	Anxiety (n = 91)	No anxiety (n = 71)	
Lifetime substance use disorder			
Alcohol abuse, %	68.9	34.1	0.043 ^a
Alcohol dependence, %	74.1	25.9	0.040 ^a
Drug abuse, %	56.8	43.2	0.935 ^a
Drug dependence, %	58.3	41.7	0.817 ^a
Lifetime psychosis, %	60.7	39.3	0.021 ^a
Rapid cycling, %	68.9	31.1	0.027 ^a
Age of onset, mean (SD)	24.8 (12.1)	25.0 (11.9)	0.900 ^b
Hospitalizations, mean (SD)	3.3 (3.0)	4.4 (4.5)	0.193 ^b
Suicide attempts, mean (SD)	2.3 (2.4)	1.2 (1.4)	0.007 ^b
GAF score, mean (SD)	60.6 (13.1)	65.6 (13.5)	0.018 ^b

^aChi-square test; ^bANOVA test for heterogeneity

patients who suffered from anxious melancholia.³⁴ In this same vein, the risk of suicide is increased in patients with unipolar depression and anxiety.^{4,21} The psychological pain associated with anxiety comorbidity in BD patients, expressed through lower scores in this quality-of-life domain, may be one of the variables influencing the higher rates of suicide attempts. It is reasonable to suppose that anxiety not only adds psychological suffering to patients with depression but may also even change the nature of the illness.³⁵ Our study's results support the notion that patients with BD who suffer from anxiety disorders are less satisfied with their lives and present more severe psychopathology.

BD patients who are not euthymic tend to present combined symptoms of depression, anxiety, and physical unrest.^{36,37} Applying Ockham's razor, one may conclude that the symptoms of "manic-depressive" patients should be attributed to mania or depression until the contrary is proven. However, the literature rooted in the lore of general practitioners suggests that symptoms of anxiety and depression are very difficult to tease apart.³⁸ Our findings are in line with these ideas. We found that the presence of anxious comorbidity correlated negatively with scores in the psychological and social domains of quality of life. However, when depression was controlled for, anxiety presented an independent effect only within the psychological domain of quality of life.

Our results showed a trend toward the association of anxiety comorbidity and poorer quality of life within the social

domain. The data show that the deleterious effect of anxiety comorbidity in the social domain of the WHOQOL was influenced by the level of depression, but a trend indicates that this effect may also exist independent of it. This suggests that the added burden of anxiety may induce further damage in the way patients perceive their social lives. Acute episodes, as well as the burden of continuous subsyndromal symptoms, are likely to jeopardize social relationships.³⁹

These results should be interpreted in the context of 3 significant limitations. First, other factors may influence quality of life, because it is a broad concept. To reduce confounders, results were adjusted for age, sex, and family income, as well as for current depressive status. Further, in a previous study regarding other factors possibly associated with lower quality of life,⁴⁰ MacQueen et al found no significant differences in quality of life scores between BD I patients with and without psychosis. In studies examining alcohol dependence, quality of life seems to improve with a good response to treatment among these patients. Second, inherent to a cross-sectional design, only associations can be inferred from the data; no causative evidence can be taken. The severity of bipolar illness can increase susceptibility to comorbidity such as anxiety and can also decrease overall quality of life. Similarly, anxiety comorbidity may contribute to an adverse course of BD and lower quality of life. A recent prospective study confirmed previous data showing that anxiety comorbidity was associated with an adverse course of BD and decreased quality of

life.²⁶ Third, although they have been combined here, not all anxiety disorders are alike. The limited number of subjects with each subtype of anxiety disorder precluded meaningful stratifications.

Despite these limitations, our study has essential strengths. It is the first study to use the WHOQOL-BREF to examine the impact of anxiety comorbidity in a sample of patients with BD. This instrument has undergone rigorous international development and is available in a wide variety of languages. It has been validated in Portuguese with a Brazilian sample. The WHOQOL-BREF uses a broader concept of quality of life than other previously frequently used scales, which had more specific concepts of health-related quality of life. Another core aspect of our study is the anxiety comorbidity diagnosis, which was accurately assessed with the SCID-I. To date, only a few studies have examined quality of life in BD patients with anxiety comorbidity. Our study confirms previous results highlighting the deleterious impact of anxiety comorbidity in BD.

In conclusion, the present study suggests that anxiety comorbidity may worsen the quality of life in patients with BD, particularly within the psychological domain. The added burden of anxiety may, in part, account for poorer outcomes, such as higher frequency of alcohol abuse, lifetime psychosis, increased number of suicide attempts, and rapid cycling. Despite the fair amount of evidence for the clinical relevance of BD–anxiety comorbidity, there are limited data focusing on the therapeutic management of patients with comorbid BD and anxiety.⁴¹ Further studies may help to validate interventions tailored to lessen the burden for BD patients who suffer from anxiety comorbidity.

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Résumé : La comorbidité de l'anxiété et la qualité de vie chez les patients souffrant de trouble bipolaire

Objectif : Évaluer l'effet de la comorbidité de l'anxiété sur la qualité de vie des patients souffrant de trouble bipolaire (TB).

Méthodes : Nous avons entrepris une étude transversale de 162 patients externes souffrant de TB, à l'aide de l'entrevue clinique structurée du DSM-IV. La principale mesure du résultat était la qualité de vie, évaluée au moyen de l'instrument de mesure de la qualité de vie en 26 items de l'OMS (WHOQOL-BREF).

Résultats : La comorbidité de l'anxiété chez les patients souffrant de TB était associée avec des scores faibles dans tous les domaines de la qualité de vie. L'effet de la comorbidité de l'anxiété sur le domaine psychologique du WHOQOL-BREF se maintenait, même quand le niveau actuel de dépression était ajouté au modèle comme facteur de confusion. La comorbidité de l'anxiété actuelle était aussi associée avec l'abus et la dépendance à l'alcool de durée de vie, les cycles rapides, la psychose de durée de vie, le nombre de tentatives de suicide, et un score faible à la mesure de l'évaluation globale du fonctionnement.

Conclusion : Nos résultats suggèrent que la comorbidité de l'anxiété chez les patients souffrant de TB est liée à une moindre qualité de vie, particulièrement dans le domaine psychologique. La comorbidité TB et anxiété peut être associée avec des marqueurs de la gravité de la maladie comme le nombre de tentatives de suicide, les cycles rapides, l'alcoolisme de durée de vie et la psychose. La reconnaissance et le traitement de la comorbidité de l'anxiété peuvent aider à soulager la souffrance psychologique des patients souffrant de TB et améliorer leur qualité de vie globale.