Suicidal Behavior in Bipolar Disorder: What Is the Influence of Psychiatric Comorbidities?

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Objective: To assess the frequency of some psychiatric comorbidities found to be associated with suicidal behavior in previous studies and to evaluate their influence on suicidal behavior in a sample of patients with bipolar disorder.

Method: We assessed 239 bipolar patients from January 2005 to January 2007. Axis I diagnosis was performed according to the DSM-IV using a structured interview (the Mini-International Neuropsychiatric Interview-Plus), and borderline personality disorder was assessed using the Structured Clinical Interview for DSM-IV Axis II Personality Disorders. Lifetime suicide history was assessed using a semistructured interview in addition to a review of medical records.

Results: There were 99 patients (41.4%) with a history of previous suicide attempts. The psychiatric comorbidities associated with suicidal behavior were borderline personality disorder (χ^2 = 36.008, p = .0001), panic disorder (χ^2 = 5.537, p = .019), alcoholism (χ^2 = 12.820, p = .001), other drug addictions (χ^2 = 10.055, p = .02), generalized anxiety disorder (χ^2 = 10.216, p = .001), and smoking (χ^2 = 9.070, p = .003). However, when logistic regression analyses were used, only the diagnosis of borderline personality disorder remained significant (Wald χ^2 = 19.13, p = .0001). When analyzing the subtypes of suicide attempts, we found that borderline personality disorder and alcoholism were associated with violent suicide attempts.

Conclusion: A diagnosis of borderline personality disorder or alcoholism (only for violent subtype of suicidal behavior) was the only comorbidity independently associated with suicide in patients with bipolar disorder. For suicide prevention, screening to identify patients at high risk for suicidal behavior should be performed routinely in patients with bipolar disorder.

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Bipolar disorder is considered to be the psychiatric diagnosis most frequently associated with suicidal behavior.[1] The suicide rate among the bipolar population is approximately 1% annually, about 60 times higher than among the general population, in which the rate is about 0.015%. Suicidal acts in patients with bipolar disorder also have higher lethality, as shown by a much lower ratio of attempted/completed suicides (approximately 3:1) than that found in the general population (approximately 30:1).[2] Furthermore, nearly one third of bipolar patients acknowledge at least 1 suicide attempt.[3]

The higher rates of suicidal behavior in bipolar disorder could be explained, at least partially, by its frequent association with other psychiatric diagnoses.[4–7] In fact, comorbidities are the rule rather than the exception in bipolar disorder, and perhaps no other Axis I psychiatric diagnosis has a higher comorbidity rate than bipolar disorder. A study carried out in academic health centers indicated that 65% of bipolar patients had at least 1 comorbid psychiatric diagnosis.[8] Comparing bipolar disorder and unipolar depression, for instance, the former has a higher prevalence of borderline personality disorder (30%–50% vs. 31.6%),[9] alcoholism (50%–60% vs. 27.2%),[4,10,11] and panic disorder (10.6%–62.5% vs. 10%).[4,10,11]

Although many studies have examined the association between suicide and psychiatric comorbidities in bipolar disorder,[4–7,12–18] only a few studies have assessed personality disorders,[6,17,18] and only 1 of them[6] specifically studied borderline personality disorder. In that study,[6] however, the authors did not mention other Axis I comorbidities and did not analyze suicidal behavior in terms of the subtype—violent or nonviolent.

This paucity of data needs to be overcome for a number of reasons. First, patients with borderline personality disorder are known to have a high rate of suicide attempts[19] and high impulsivity scores,[20] a common phenotype in suicidal patients.[21] Second, borderline personality disorder is the Axis II diagnosis most frequently associated with psychiatric comorbidities.[22] Even if it is frequently underrecognized,[23] borderline personality disorder occurs in about 20% of the population in psychiatric settings.[19] It is possibly the Axis II diagnosis most frequently associated with mood disorders, as about 90% of borderline patients have unipolar depression and 10% have bipolar disorder.[24] A recent study[25] found that the prevalence of bipolar disorder in a borderline patient sample was 19.4%; in addition, after 4 years of follow-up, only 4% of them had new onset of bipolar disorder.[25]

Finally, several studies have found a childhood history of trauma, particularly sexual abuse, which could cause damage to patients' mechanisms of resilience and stress response.[19] As a consequence, these patients would have inappropriate and higher reactivity to stressors, manifested by impulsivity, hostility, emotional instability, and lack of identity.[23] These data taken together strongly suggest that a comorbid diagnosis of borderline personality disorder could contribute considerably to suicidal behavior in patients with bipolar disorder.

In this study, we aimed to evaluate psychiatric comorbidities in a well-characterized sample of bipolar patients. The main objective of our study was to clarify the role of those comorbidities, particularly borderline personality disorder, in suicidal behavior of bipolar patients.

METHOD

We studied 239 bipolar patients, subtype I and II, consecutively admitted from January 2005 to January 2007 as inpatients or outpatients in a psychiatric unit specializing in the treatment of bipolar disorder. Patients in a euthymic state were diagnosed according to DSM-IV criteria on the basis of a structured interview (the Mini-International Neuropsychiatric Interview-Plus)[26] by a psychiatrist. The patients were considered to be euthymic, based on clinical judgment, when they were free of acute symptoms and had the cognitive ability to answer the survey. For the purpose of our study, we assessed lifetime history of psychosis and only the comorbidities that had been consistently associated with suicide in past studies[4–7]: generalized anxiety disorder, panic disorder, borderline personality disorder, alcoholism, other drug dependence, and smoking. Furthermore, we excluded any comorbidity with less than 5% prevalence in our sample. When we followed this rule, cluster A, cluster C, and other cluster B disorders were excluded (histrionic, narcissistic, and antisocial personality disorders). Diagnosis of borderline personality disorder was performed using the Structured Clinical Interview for DSM-IV Axis II Personality Disorders.[27] The term *drug addictions* used in our study encompasses cannabis and cocaine addiction, because all cocaine-dependent patients had a history of cannabis dependence. The number of patients with only cannabis lifetime dependence was not enough to justify a separate analysis. Finally, opiate addiction is rare in our country, and no patient in our sample had this addiction.

History of suicide attempt was assessed using a semi-structured interview in addition to a review of medical records, as previously described.[28,29] Furthermore, a supplementary interview with at least 1 close family member was performed in order to confirm the patient's information. A suicide attempt was defined as a conscious intent of the patient to end his or her life, even if ambivalent, through means that the patient believed could result in death.[30] A suicide attempt was characterized as violent or nonviolent in accordance with the methods used. Hanging, profound cutting, and jumping from a considerable height were considered violent methods, while taking poison or pills was not considered a violent method. Patients who had multiple suicide attempts were considered as using violent methods only if at least 1 violent suicide attempt was performed.

All procedures were approved by the local ethics committee and were in accordance with the Helsinki Declaration of 1975. All participants signed an informed consent form after a full explanation of the study.

Statistical analysis was done by a χ^2 test for categorical data. Differences between groups were assessed with a Student t test. A multiple logistic regression analysis was performed to control for possible confounding factors. Tests were 2-tailed, and results were considered significant when $p \leq .05$.

RESULTS

In our sample of 239 patients with bipolar disorder, we observed that 99 (41.4%) had a lifetime history of suicide attempts. Patients were subgrouped according to their suicide attempt history and evaluated according to their sociodemographic and clinical characteristics. We observed that those attempting suicide were younger than those not attempting suicide (age, mean ± SD: 38.1 ± 12.2 years; $t = 4.107$, $p = .0001$), had their first depressive episode about 6 years before those not attempting suicide (age, mean ± SD: 24.8 ± 9.6 years vs. 30.6 ± 12.8 years; $t = 3.048$, $p = .003$), and had their first manic episode 4.6 years before those not attempting suicide (age, mean ± SD: 21.0 ± 8.5 years vs. 25.6 ± 12.7 years; $t = 3.783$, $p = .0001$). Furthermore, those attempting suicide had a history of more frequent hospitalizations ($\chi^2 = 9.221$, $p = .002$), comorbidities ($\chi^2 = 14.467$, $p = .0001$), higher number of manic episodes (mean ± SD: 13.6 ± 11.5; $t = –3.944$, $p = .0001$), and

Table 1. Clinical and Sociodemographic Characteristics of the Study Population[a] According to History of Suicide Attempt

Clinical or Sociodemographic Factor	History of Suicide Attempt, Mean ± SD or N (%) Yes, N = 99 (41.4%)	No, N = 140 (58.6%)	χ^2 or t Statistic	p Value
Age, y	38.1 ± 12.2	45.0 ± 12.5	t = –4.107	.000
Gender, female (N = 171)	75 (43.8)	96 (56.2)	χ^2 = 1.471	.225
Marital status, single (N = 98)	36 (36.7)	62 (63.3)	χ^2 = 7.513	.185
Currently working (N = 35)	11 (31.4)	24 (68.6)	χ^2 = 4.981	.429
Education, > 8 years (N = 104)	50 (48.1)	54 (51.9)	χ^2 = 6.820	.234
Bipolar I diagnosis (N = 152)	56 (36.8)	96 (63.2)	χ^2 = 9.692	.021
Age at first depressive episode, y	24.8 ± 9.6	30.6 ± 12.8	t = –3.048	.003
Age at first manic episode, y	21.0 ± 8.5	25.6 ± 12.7	t = 3.783	.000
History of hospitalization (N = 173)	82 (82.8)	91 (65.0)	χ^2 = 9.221	.002
History of comorbidities (N = 195)	92 (92.9)	103 (73.6)	χ^2 = 14.467	.000
Age at first hospitalization, y	26.1 ± 11.3	24.7 ± 17.5	t = 0.649	.517
Number of manic episodes	13.6 ± 11.5	7.6 ± 8.2	t = 3.944	.000
Number of depressive episodes	8.7 ± 6.8	4.3 ± 4.9	t = 4.864	.000
Lifetime history of psychosis (N = 49)	22 (44.9)	27 (55.1)	χ^2 = 0.307	.580

[a]239 patients with DSM-IV bipolar I or bipolar II disorder.

Table 2. History of Suicide Attempt Related to Comorbidity in 239 Patients With Bipolar Disorder

Comorbidity	N (%)	History of Suicide Attempt, N (%) No (N = 140)	Yes (N = 99)	χ^2 Statistic	p Value
Panic disorder	50 (20.9)	22 (44.0)	28 (56.0)	5.537	.019
Generalized anxiety disorder	106 (44.4)	50 (47.1)	56 (52.9)	10.216	.001
Borderline personality disorder	49 (20.5)	10 (20.5)	39 (79.5)	36.008	.000
Smoking	122 (51.0)	60 (49.1)	62 (50.9)	9.070	.003
Alcoholism	67 (28.0)	27 (40.3)	40 (59.7)	12.820	.001
Other drug addiction	33 (13.8)	11 (33.3)	22 (66.7)	10.055	.020
Without comorbidity	44 (18.4)	37 (84.1)	7 (15.9)	14.467	.000

Table 3. Logistic Regression Analysis for Association of Comorbidity and Suicide Attempt in Bipolar Patients

Covariant	B	Standard Error	Wald χ^2	p Value	Odds Ratio
Panic disorder	0.295	0.381	0.593	.440	1.341
Borderline personality disorder	1.798	0.411	19.139	.000	6.042
Smoking	0.505	0.318	2.543	.114	1.660
Alcoholism	0.308	0.373	0.692	.410	1.363
Other drug addiction	0.551	0.470	1.361	.243	1.731
Generalized anxiety disorder	0.345	0.307	1.269	.260	1.412

Table 4. Logistic Regression Analysis for Association of Comorbidity and Suicide Attempt Classification (violent vs. nonviolent) in Bipolar Patients

Covariant	B	Standard Error	Wald χ^2	p Value	Odds Ratio
Panic disorder	0.537	0.505	1.130	.288	1.710
Borderline personality disorder	2.530	0.515	24.165	.000	12.557
Smoking	0.194	0.490	0.156	.693	1.214
Alcoholism	1.135	0.526	4.656	.031	3.112
Other drug addiction	0.234	0.621	0.142	.706	1.264
Generalized anxiety disorder	0.340	0.454	0.561	.454	1.405

higher number of depressive episodes (mean ± SD: 8.7 ± 6.8; t = 4.864, p = .0001) than those not attempting suicide. We did not find an association between lifetime history of psychosis and suicide (χ^2 = 0.307, p = .580) (Table 1).

A lifetime psychiatric comorbidity was observed in 195 (81.6%) of the 239 patients we studied. The most prevalent diagnoses were smoking (51.0%), generalized anxiety disorder (44.4%), alcoholism (28.0%), panic disorder (20.9%), borderline personality disorder (20.5%), and other drug addiction (13.8%). We observed that all comorbidities were significantly more frequent in those attempting suicide than in those not attempting suicide (Table 2). However, the only comorbidity that maintained statistical significance after logistic regression analysis was a diagnosis of borderline personality disorder (Table 3).

We further subgrouped suicide attempts according to type: violent or nonviolent. All comorbidities were significantly more frequent in patients with a history of a violent suicide attempt as compared to those with nonviolent suicide attempts: generalized anxiety disorder (χ^2 = 12.087, p = .002), borderline personality disorder

Table 5. Comparison of Clinical and Sociodemographic Characteristics Between Bipolar Patients With and Without Borderline Personality Disorder (N = 239)

Clinical or Sociodemographic Factor	Borderline Personality Disorder, Mean ± SD or N (%): Yes (N = 49)	Borderline Personality Disorder, Mean ± SD or N (%): No (N = 190)	χ^2 or t Statistic	p Value
Age, y	35.2 ± 10.5	43.8 ± 12.7	t = –4.333	.000
Gender, female (N = 171)	40 (81.6)	131 (68.9)	χ^2 = 3.079	1.079
Marital status, single (N = 98)	17 (34.7)	81 (42.6)	χ^2 = 9.955	.077
Currently working (N = 35)	5 (10.2)	30 (15.8)	χ^2 = 7.122	.212
Education, > 8 years (N = 104)	26 (53.1)	78 (44.1)	χ^2 = 4.528	.048
History of comorbidities (N = 191)	45 (91.8)	146 (76.8)	χ^2 = 5.457	.019
Having > 2 comorbidities (N = 70)	30 (61.2)	40 (21.1)	χ^2 = 30.353	.000
Bipolar I diagnosis (N = 152)	24 (49.0)	128 (67.4)	χ^2 = 12.483	.006
Age at first depressive episode, y	20.1 ± 7.8	24.5 ± 12.0	t = –2.905	.004
Age at first manic episode, y	24.2 ± 10.3	29.3 ± 12.1	t = –2.581	.011
History of hospitalization (N = 173)	43 (87.8)	130 (68.4)	χ^2 = 7.285	.007
Age at first hospitalization, y	25.4 ± 12.9	25.3 ± 15.7	t = 0.016	.987
Number of manic episodes	14.4 ± 12.3	9.0 ± 9.1	t = 2.529	.015
Number of depressive episodes	8.6 ± 6.6	5.6 ± 5.9	t = 2.660	.009
Total number of manic and depressive episodes	24.2 ± 17.0	14.8 ± 13.1	t = 3.064	.004
Number of comorbidities	3.8 ± 1.6	1.5 ± 1.2	t = 9.161	.000
Number of suicide attempts	2.8 ± 2.2	0.7 ± 1.3	t = 6.364	.000

(χ^2 = 52.147, p = .0001), panic disorder (χ^2 = 10.086, p = .006), smoking (χ^2 = 8.608, p = .014), alcoholism (χ^2 = 21.933, p = .0001), and other drug addictions (χ^2 = 10.656, p = .005). A logistic regression analysis was also done, and we were able to show that only 2 comorbidities remained statistically significant in their association with violent suicide attempts: borderline personality disorder and alcoholism (Table 4).

We performed additional analyses in order to best clarify how bipolar patients with comorbid borderline personality disorder are different from bipolar patients without this comorbidity (Table 5). We found that in the borderline group, the patients were about 8 years younger (age, mean ± SD: 35.2 ± 10.5 years vs. 43.8 ± 12.7 years; t = –4.333, p = .0001), were predominantly female (χ^2 = 3.079, p = .079), had another additional psychiatric diagnosis (χ^2 = 5.457, p = .019), had bipolar type I diagnosis (χ^2 = 12.483, p = .006), experienced their first depressive episode about 4 years earlier (age, mean ± SD: 20.1 ± 7.8 years vs. 24.5 ± 12.0 years; t = –2.905, p = .004), experienced their first manic episode 5 years earlier (age, mean ± SD: 24.2 ± 10.3 years vs. 29.3 ± 12.1 years; t = –2.581, p = .011), and had more frequent history of hospitalization (χ^2 = 7.285, p = .007). The borderline patients had a higher number of manic episodes in their lifetime (mean ± SD: 14.4 ± 12.3 vs. 9.0 ± 9.1; t = 2.529, p = .015), a higher number of depressive episodes (mean ± SD: 8.6 ± 6.6 vs. 5.6 ± 5.9; t = 2.660, p = .009), a higher number of comorbidities (mean ± SD: 3.8 ± 1.6 vs. 1.5 ± 1.2; t = 9.161, p = .0001), and a higher incidence of suicide attempts (mean ± SD: 2.8 ± 2.2 vs. 0.69 ± 1.3; t = 6.364, p = .0001).

DISCUSSION

The most important result of our study—constituting its novelty—was the fact that we were able to show that borderline personality disorder, but not the other studied comorbidities, was independently associated with suicide attempts in patients with bipolar disorder. Still, some points deserve more detailed discussion.

Confirming previous studies, we were able to show that in our sample, patients with bipolar disorder had a high frequency of psychiatric comorbidities.[4–7,12–18] Furthermore, in accordance with the literature,[4–7,31] we found a higher frequency of suicide attempts in bipolar patients suffering from panic disorder, generalized anxiety disorder, alcoholism, other drug addiction, smoking, and borderline personality disorder. We were not able to show the same association with a history of psychosis. Nevertheless, among all the statistically significant associations mentioned above, borderline personality disorder was the only comorbidity independently associated with suicide attempts. Smoking has been studied as a psychiatric comorbidity in a recent study.[7] A positive association was found between this condition and suicidal behavior in bipolar disorder; however, the results reported by that study should be interpreted cautiously because the authors do not assess other disorders related to suicide and smoking, such as a borderline personality disorder diagnosis.

We further investigated the association between the type of suicide attempt—violent or nonviolent—and comorbidities. We consider this distinction important since suicidal behavior is a complex phenomenon with biological, environmental, developmental, and learned contributing factors. In view of this multideterminism, a

more specific, phenotypic characterization of suicide attempts is of major interest, given that some factors could play a major role in select categories of suicidal behavior (e.g., violent attempts) but not in others. For instance, we recently showed that a functional polymorphism in the serotonin transporter was associated with violent suicide attempts, but not with all suicide attempts.[32] In the same way, we speculate that some comorbidities could play a role in select types of suicidal behavior but not in others. We found a higher frequency of violent suicide attempts in bipolar patients having each comorbidity studied, with the exception of a history of psychosis. However, only 2 comorbidities were independently associated with violent suicide attempts. Again, we found a strong association with borderline personality disorder ($p < .0001$) and, new to this study, an association with alcoholism ($p = .03$), although the latter was far weaker.

We have also shown that demographic factors such as marital status, children, years of education, and current work status had no influence on suicide attempts in the population studied. Interestingly, a recent meta-analysis[33] of only prospective studies found similar results. This finding suggests that factors related to bipolar disorder itself (e.g., genetic, clinical), different from those observed in other diagnosis groups,[34,35] are possibly more important than sociodemographic parameters in explaining the suicidal behavior of these patients.

In our study, 41.4% of the bipolar patients had made at least 1 suicide attempt. This rate was most likely high, principally because our patients were relatively young—about 41 years old. However, studies carried out in inpatient units also tend to include more suicidal patients, in part because potential reasons for admission include suicide risk or a recent suicide attempt. Our sample was 95% composed of inpatients or outpatients assessed a month or less after discharge. Another point that must be considered, and which, in our view, constituted the strength of our study, was that we assessed suicidal behavior using a semistructured interview as well as a supplementary interview with at least 1 close family member, in addition to a review of medical records. This is an important point since it has previously been shown that a significant degree of past suicidal behavior is not usually recorded during routine clinical assessment.[36] The use of semistructured screening may improve documentation and detection of lifetime suicidal behavior.[37]

The concept of comorbidity has been an object of controversy within our current nosologic classification system. From an epidemiologic point of view, the term *comorbidity* means "any distinct additional clinical entity that has existed or that may occur during the clinical course of a patient who has the index disease under study,"[38(p456)] and it should be a separate disease entity not better accounted for by heterotypic continuity or phenotypically overlapping syndromes.[39] The boundaries between psychiatric diseases, however, are not well defined.[40] Additionally, the coexistence of 2 or more diagnoses is more frequent than a single diagnosis,[41,42] so comorbidity may be only an artifact produced by our nosology, which is largely based on phenomenology.[43]

Above and beyond this discussion, from the clinical point of view, some authors believe that although the concept of comorbidity cannot be supported by the current knowledge of etiology and pathophysiology, it can be useful clinically in identifying patients who might not have a good prognosis.[44,45] Our study clearly shows that patients with bipolar disorder are likely to make more suicide attempts, particularly more violent ones, when a comorbid diagnosis of borderline personality disorder is present.

After analyzing the patients and subgrouping them according to history of borderline personality disorder diagnosis, we were astonished to find that the bipolar/borderline group, when compared with the bipolar/nonborderline group, had unfavorable clinical aspects in all parameters analyzed. These patients seem to belong to another disorder group. The number of suicide attempts is about 4 times higher in the bipolar/borderline group. Moreover, these patients "attract," because 61.2% of them have a history of 2 or more comorbidities, while only 21.1% of the nonborderline group have such a history of 2 or more comorbidities.

Considering that bipolar patients themselves have elevated aggressiveness and impulsivity scores[46] and that the same characteristics are prominent in borderline patients,[47] it is possible that the sum of severe mood episodes (the core of bipolar disorder) and high environmental reactivity (the core of borderline personality disorder) could result in an explosive mixture leading to more frequent and more violent suicide attempts.

In summary, this study showed that when analyzing patients with bipolar disorder, it is of pivotal importance to screen for borderline personality disorder in order to identify risk factors for suicidal behavior. However, there were some limitations that should be highlighted. As in all retrospective analyses, we could identify correlations between clinical factors and suicidal behavior, but this obviously did not allow us to ascertain causal relationships. Furthermore, we were not exempt from bias because it is possible that patients with a history of suicide attempts have a greater probability of being diagnosed with borderline personality disorder than do patients without a history of suicide attempts, since recurrent suicide attempts are one of the diagnostic criteria for borderline personality disorder. However, a study has shown that even when the self-injury item is excluded, affective instability remains strongly associated with suicidal behaviors.[48] Furthermore, all patients were assessed by an experienced psychiatrist using structured instruments for all Axis I and borderline personality disorder diagnoses.

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