Complicated Grief and Its Correlates in Patients With Bipolar Disorder

Naomi M. Simon, M.D., M.Sc.; Mark H. Pollack, M.D.; Diana Fischmann, B.A.; Carol A. Perlman, Ph.D.; Anna C. Muriel, M.D.; Cynthia W. Moore, Ph.D.; Andrew A. Nierenberg, M.D.; and M. Katherine Shear, M.D.

Background: While the recent loss of a loved one has been identified as a risk factor for suicide in patients with bipolar disorder, and complicated grief (CG) has been associated with elevated rates of suicidality compared with loss without CG, little is known about the frequency or impact of CG in bipolar disorder. We investigated the frequency and implications of loss of loved ones in an ongoing study of bipolar disorder.

Method: We conducted a survey of 120 patients with well-characterized DSM-IV bipolar disorder participating in Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), a large naturalistic study, in order to identify frequency of loss and to examine the presence of CG and its clinical correlates. Survey data were gathered from October 2003 to March 2004.

Results: A lifetime history of a significant loss was reported by 86% (103/120) of participants; 24.3% (25/103) of those met criteria for CG, defined as a score ≥ 25 on the Inventory of Complicated Grief (ICG), with a mean ± SD ICG score of 33.7 ± 6.9. The presence of CG was associated with elevated rates of panic disorder and alcohol abuse comorbidity, as well as other measures of panic symptoms and phobic avoidance. CG was also associated with a higher rate of lifetime suicide attempts, greater functional impairment, and poorer social support.

Conclusion: Our findings suggest the presence of a substantial burden of comorbid grief-related illness and impairment in patients with bipolar disorder. Further research is needed to understand the overlap of anxiety disorders and phobic avoidance in bipolar patients with complicated grief.

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Corresponding author and reprints: Naomi M. Simon, M.D., Center for Anxiety and Traumatic Stress Disorders, Massachusetts General Hospital, Simches Research Building, 2nd Floor, 185 Cambridge Street, Boston, MA 02114 (e-mail: nsimon@partners.org).

Loss of a loved one is well known to be among the most severe life stressors. It is also widely known that for a group of bereaved people, grief can become a chronic, debilitating state. Yet, there is little information regarding the prevalence or outcome of bereavement in seriously mentally ill patients. Recently, investigators have identified a clinically significant grief reaction, designated *traumatic grief* or *complicated grief* (CG). This condition is a source of substantial distress and has been associated with impaired quality of life, poor medical outcomes, and suicidality.[1,2] Although CG is not yet a formal psychiatric diagnosis in the DSM and is still defined somewhat variably in the literature, there is a growing consensus about its core elements, which include unrelenting grief persisting 6 or more months after the loss, with symptoms of separation distress (including persistent yearning, preoccupation with and longing for the deceased, and an inability to accept the death), traumatic distress (including intrusive reliving and avoidance of reminders of the deceased), and difficulty adapting to the loss.[3–7]

Some information is available regarding co-occurrence of CG with other DSM-IV disorders. Complicated grief has been shown to be distinct from depression and posttraumatic stress disorder,[8,9] though rates of comorbidity with these conditions are high.[9] In a recent publication, 30% of those with CG met criteria for panic disorder.[9] Bipolar disorder has been reported comorbid with CG[9,10]; however, we could find no report of the prevalence or impact of CG among patients with bipolar disorder. The recent loss of a loved one and poor social support have been identified as proximal risk factors for suicide attempts[11] in patients with bipolar disorder. Given the high rates of suicide in bipolar disorder, it is imperative to begin to identify and modify relevant risk factors.

Among elderly patients,[12] adolescents,[13] and bereaved people in the community,[14] individuals with CG report a significantly higher rate of suicidal ideation than bereaved people without this condition. We recently found that patients who present for treatment of CG have a high rate of suicidal ideation and behaviors (K. Szanto, M.D.; M.K.S.; P. Houck, M.Stat., et al., manuscript submitted). We predicted that among individuals with bipolar dis-

order, CG would be associated with suicidality, compared with loss of a loved one without development of CG. We further hypothesized that the presence of CG in bipolar disorder would be associated with higher rates of panic disorder, greater impairment, and a greater overall burden of comorbid anxiety symptoms and disorders.

METHOD

This investigation is part of a larger study of predictors of suicidality, designed as an ancillary project to the multicenter, National Institute of Mental Health–funded naturalistic study of bipolar disorder, Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). Details of the methodology of STEP-BD, from which our patients were recruited, have been published elsewhere.[15] STEP-BD sites enrolled patients seeking clinical care who were willing to undergo longitudinal clinical assessments; participation in the study did not alter care by their physicians or change the fee structure for their visits to the clinic.[16] Because our study was ancillary to STEP-BD, data available already within the clinical study, such as demographic data and diagnosis, were not collected again but were provided from the STEP-BD database; thus, the relevant methods of STEP-BD are briefly described here.

In STEP-BD, information about age, gender, marital status, race, and education are collected using a demographics form at study entry. Participants undergo clinician interviews every 12 months, using the Mini-International Neuropsychiatric Interview (MINI Plus Version 5.0)[17] adapted to additionally assess lifetime anxiety and eating disorders. In addition, current clinical bipolar status based on the presence or absence of DSM-IV–based criteria is assessed in this naturalistic study at every clinical visit (varying in frequency by clinical need) utilizing a Clinical Monitoring Form. Patients achieving relative euthymia (≤ 2 moderate symptoms of depression or mania/hypomania) for at least 1 week are assigned a status of recovering or recovered, depending on whether this status has been sustained for at least 8 weeks. These bipolar state categories and interrater reliability training are further discussed by Sachs et al.[15] For the current study, all comorbidity diagnostic information was derived from the most recent MINI, which was completed a mean ± SD of 12.5 ± 9.4 months prior to questionnaire completion. Current bipolar status was assessed at the most recent clinical visit, a mean of 1.6 ± 2.5 months prior to questionnaire completion.

All active participants from the Massachusetts General Hospital (MGH) site of STEP-BD as of Sept. 23, 2003, (N = 258) were mailed the study questionnaire packet on Oct. 23, 2003. The packet contained a cover letter requesting that they complete the questionnaires for a study examining predictors of "the relationship between anxiety symptoms, bipolar disorder and suicidality" and informing participants that upon our receipt of the returned packet, they would be compensated $30 for their time. The MGH Institutional Review Board approved study procedures. The packet included the Inventory of Complicated Grief (ICG),[4] a 19-item self-rated scale that assesses symptoms of CG associated with the death of a loved one. We added a cover sheet to the ICG that asked the following questions about loss: "Have you ever had a close relative or significant other pass away?" and "What year did the person die?" Those with a loss were asked to identify their relationship to the deceased and the year of death and to complete the ICG. A score of 25 or more 6 months after a death can be used to discriminate the presence of CG and associated impairment.[1,4] We thus defined CG as a score of 25 or greater on the ICG, concurrent with a reported loss occurring at least 6 months prior to assessment.

Social support was assessed with the Multidimensional Scale of Perceived Social Support,[18] a 12-item measure of an individual's appraisal of the presence of unconditional, nonjudgmental emotional support rated on a 7-point Likert scale from 1 ("very strongly disagree") to 7 ("very strongly agree"). We measured the presence of current panic attacks and their severity using the first 2 items of the validated self-rated Panic Disorder Severity Scale (PDSS-SR).[19,20] Because of previous work suggesting a significant impact of panic symptoms on bipolar outcomes,[21,22] we also administered a standard measure of phobic avoidance, the Marks Fear Questionnaire,[23] as well as the Panic-Agoraphobic Spectrum Self-Report Scale (PAS-SR), a previously validated[24] 114-item questionnaire with 8 domains assessing lifetime symptoms including separation sensitivity, somatic fears, anxiety about medications, and avoidance of stimuli[25] with specific subscales.[26] In addition, we administered the Range of Impaired Functioning Tool (LIFE-RIFT),[27] a clinician-rated scale that provides a brief measure of functional impairment.

Participants also completed a questionnaire measure of lifetime suicide attempts, including their age at the time of their most serious attempt and the lifetime number of suicide attempts.

Analyses

For univariate analyses, the Fisher exact test (FET) was used for categorical measures, while 2-sided t tests were used for group comparisons of continuous measures. Because prior data support links between panic and suicidality in bipolar disorder, and clear prediction of phobic avoidance by anxiety disorders, we were interested in assessing the independent impact of CG on these outcomes; we thus used focused linear and logistic regression modeling approaches, respectively. Significance was set at the .05 level for all tests, without correction for multiple testing; all test results are provided for the reader.

RESULTS

Frequency and Impact of Loss

Of 258 patients contacted for potential participation, we received 120 completed study packets (46.5%). Sixty-two percent of the sample had a bipolar I diagnosis, with a mean ± SD duration of illness of 26.9 ± 12.7 years. Participants were 59% women, with a mean ± SD age of 44.1 ± 13.3 years, and 95% were white. Eighty-six percent (103/120) of respondents reported a lifetime history of a significant loss and completed the ICG, with the most recent reported loss occurring 12.3 ± 11.3 years prior. More than 1 loss was reported by 38.8% (40/103) of respondents. There was no difference in demographics for those with and without a loss. A significantly greater proportion of those with a lifetime loss than those without a loss were in a current mood episode (35% vs. none; FET p = .003). Further, there was greater functional impairment as measured by the LIFE-RIFT for those with a loss (t = 3.2, df = 115, p = .0017). However, there was no significant difference in the prevalence of anxiety disorder or substance use disorder current or lifetime comorbidity, or history of suicide attempts.

Complicated Grief Among Patients With Bipolar Disorder

Among the 103 respondents reporting a loss, 24.3% (25/103) met ICG criteria for CG, with a mean ± SD ICG score of 33.7 ± 6.9 (range, 25–46). More than 1 loss was reported by 60% of the CG sample (15/25), compared with 40% (31/78) of those without CG (FET p = .11). There was no difference in the nature of the relationships to the deceased among those with and without CG. For those with CG, losses included parent 52% (13/25), grandparent 52% (13/25), spouse/significant other 12% (3/25), sibling 28% (7/25), other person or relative 24% (6/25), friend 16% (4/25), and pet 4% (1/25). For those without CG, losses included parent 56% (44/78), grandparent 44% (34/78), spouse/significant other 4% (3/78), sibling 8% (6/78), other person or relative 17% (13/78), friend 13% (10/78), and pet 1% (1/78). In the CG sample, the most recent reported death occurred a mean ± SD of 8.0 ± 8.0 years ago (range, 1–37 years), while for those without CG the most recently reported loss was 13.8 ± 11.9 years ago (range, 1–53 years) (t = 2.3, df = 101, p < .03).

Complicated Grief in Bipolar Patients: Demographics, Mood State, and Quality of Life

There was no difference in the CG group compared with the no CG group in the following variables, which are presented for the full sample of those with a reported loss (N = 103): age (mean ± SD = 46.4 ± 12.7 years), gender (60.2% women), marital status (36% currently married, 32% never married), education (72% with bachelor's or graduate/professional school degree), race (96% white), duration of bipolar diagnosis (mean ± SD = 29.2 ± 12.1 years), or bipolar subtype (65% bipolar I). Most study participants were not in a current mood episode, with 65% of patients rated as "in recovery or recovering" by their study clinician at the most recent visit and no significant difference based on the presence of CG (56%) compared with no CG (68%). Overall, fewer than 5% (N = 5) of participants were in a current manic, hypomanic, or mixed episode, and 18.5% (N = 19) currently met criteria for a major depressive episode. Among those who had lost someone close, the presence of CG carried an association with poorer functioning, as measured by the LIFE-RIFT, and poorer levels of social support, as measured by the Perceived Social Support Scale (Table 1).

Suicidality and Complicated Grief in Patients With Bipolar Disorder

In the CG sample, more patients reported a lifetime history of a suicide attempt (58.3% vs. 33.8%), which reached the level of a statistical trend in univariate analyses (FET p = .054). This association of CG with suicide attempts did not diminish after controlling for lifetime panic disorder, with a more than doubling of the odds of a lifetime suicide attempt (OR = 2.5, Z = 1.92, p < .06). Although power is limited by sample size, there was no significant interactive effect of panic with CG in the model of lifetime suicide attempts, suggesting independent and additive effects of CG and panic in suicide attempts. This point is illustrated by the findings that lifetime suicide attempts were reported for 31% (19/62) of patients without CG or panic, 44% (7/16) of those with panic but not CG, 53% (8/15) of those with CG but not panic, and 70% (7/10) of those with both disorders. A greater percentage of patients who experienced a loss and had CG made multiple suicide attempts (34.8%) compared with those without CG (12.0%; FET p = .034). However, there was no significant difference in the number of years since the last attempt (mean ± SD = 12.8 ± 12.3 years). Interestingly, though, for 7 of the 14 patients with CG who reported dates of suicide attempts, their most recent attempt occurred before the first reported loss.

Comorbidity With Complicated Grief in Bipolar Patients: Association With Anxiety Disorders and Symptoms

As presented in Table 2 , the presence of CG was associated with higher rates of current alcohol abuse, current panic disorder with or without agoraphobia, and lifetime obsessive-compulsive disorder. Patients with CG were more than twice as likely to have more than 1 current anxiety disorder diagnosis than those without CG.

Panic-related symptoms were also more frequent among those with, compared with those without, CG. Almost two thirds (65%) of the CG sample reported current

Table 1. Complicated Grief and Its Clinical Correlates in Patients With Bipolar Disorder[a]

Measure[b]	Complicated Grief (ICG score ≥ 25)	No Complicated Grief (ICG score < 25)	t	df	p
PDSS-SR measure, N (%)					
Current full or partial panic attacks	15 (65.22)	20 (26.32)			.001[c]
At least 2 full panic attacks per week	3 (13.05)	2 (2.63)			.001[c]
PAS-SR score					
Total score	54.46 (24.56)	40.28 (22.56)	–2.63	100	.0097
Paniclike symptoms	17.96 (5.52)	13.66 (7.56)	–2.62	101	.0101
Substance and medication sensitivity	4.21 (2.64)	2.81 (2.10)	–2.68	100	.0085
Anxious expectation	3.56 (1.47)	2.55 (1.79)	–2.54	101	.0126
Agoraphobia	10.44 (6.83)	7.22 (6.05)	–2.25	101	.0270
Illness-related phobias and hypochondriasis	2.56 (1.75)	1.48 (1.57)	–2.90	100	.0046
Reassurance sensitivity	8.33 (4.64)	5.74 (4.05)	–2.65	100	.0095
Separation sensitivity	7.52 (3.79)	6.01 (3.78)	–1.73	101	.087
Marks Fear Questionnaire score					
Total phobia subscale	41.16 (22.63)	27.94 (18.49)	–2.94	100	.0041
Rating of associated anxiety and depression	24.38 (8.52)	18.21 (10.61)	–2.59	98	.0110
Global phobia rating (distress and avoidance)	4.77 (1.88)	2.49 (2.13)	–4.52	93	.0000
LIFE-RIFT score	12.50 (3.43)	9.47 (3.45)	–3.75	98	.0003
Perceived Social Support Scale score	52.24 (21.15)	63.50 (15.59)	2.87	101	.0050

[a]Values shown as mean (SD) unless otherwise noted.
[b]Group Ns differed between measures owing to missing data for some rating scales.
[c]Fisher exact test.
Abbreviations: ICG = Inventory of Complicated Grief, LIFE-RIFT = Range of Impaired Functioning Tool, PAS-SR = Panic-Agoraphobic Spectrum-Self Report Scale, PDSS-SR = self-rated Panic Disorder Severity Scale.

full or partial panic attacks on the PDSS-SR, compared with only 26% of those without CG (FET p = .001); 13% with CG reported at least 2 full attacks per week compared with only 3% without CG. Similarly, CG patients had significantly higher PAS-SR total scores, as well as higher scores on specific subscales representing paniclike symptoms, substance and medication sensitivity, anxious expectation, agoraphobia, illness-related phobias and hypochondriasis, and reassurance sensitivity (see Table 1).

The total phobic symptoms score on the Marks Fear Questionnaire was substantially elevated in the CG sample, and the global phobia score was nearly doubled compared with that in patients who lost someone close but did not develop CG (see Table 1); CG continued to significantly predict elevated total phobic avoidance in a regression model controlling for any current anxiety disorder and current mood state ($\beta = 10.2$, $t = 2.4$, $p < .02$).

DISCUSSION

We found that 86% of 120 participants drawn from a well-characterized sample of patients with bipolar disorder reported loss of a close attachment figure. This prevalence of lifetime loss is higher than rates reported by Piper and colleagues[10] in a general psychiatric outpatient sample with a similar mean age in the 40s (55%). Participants in our study were those who chose to participate in a self-report questionnaire study about anxiety and suicidality in bipolar disorder, and only 46% of eligible individuals returned study questionnaires, which had been mailed to their home address. Even though death and grief were not highlighted in our study, it is possible that an ascertainment bias was present, with a greater proportion of patients with a prior loss completing the questionnaires. Given this caveat, those who reported a lifetime loss had significantly poorer current functioning and a higher likelihood of being in a current bipolar mood episode, supporting the well-recognized importance of loss as a major stressor.

Among those who reported a significant loss, nearly 25% met ICG criteria for current CG, even though the most recent death occurred 8 years earlier. The last author observed similar chronicity of this syndrome in a recently completed study of CG.[28] Complicated grief in the bipolar sample was associated with poorer functioning and lower levels of perceived social support, indicating a substantial burden of comorbid bereavement-related illness. Those with CG were more than twice as likely to also have an anxiety disorder and in particular had significantly higher rates of current panic disorder, phobic symptoms, and panic spectrum symptoms.

The high rates of overall anxiety comorbidity and current substance use disorders we observed in association with CG suggest that CG may be a marker of a subgroup of bipolar patients with increased burden of illness. We and others have recently demonstrated a substantial negative impact of comorbid anxiety, and particularly panic, on bipolar disorder outcomes, including increased suicidality and reduced amount of time spent in relative euthymia.[21,22] However, we documented an independent and additive association of panic comorbidity and CG with lifetime suicide attempts. Our results suggest that the co-occurrence of these conditions comprises a subpopulation of bipolar patients at very high risk and often unrec-

Table 2. Complicated Grief and Additional Psychiatric Comorbidity in Patients With Bipolar Disorder

Comorbidity	Complicated Grief (ICG score ≥ 25) N (%)	No Complicated Grief (ICG score < 25) N (%)[a]	p[b]
Any anxiety diagnosis			
Current	11 (44)	22 (29)	.219
Lifetime	18 (72)	49 (63)	.475
Panic disorder with or without agoraphobia			
Current	4 (16)	2 (3)	.032
Lifetime	10 (40)	16 (20)	.065
Agoraphobia (no panic disorder)			
Current	1 (4)	2 (3)	1.00
Lifetime	3 (12)	6 (8)	.684
Social anxiety disorder			
Current	6 (24)	10 (13)	.216
Lifetime	8 (32)	21 (27)	.618
Obsessive-compulsive disorder			
Current	4 (16)	3 (4)	.061
Lifetime	6 (24)	5 (6)	.023
Posttraumatic stress disorder			
Current	5 (20)	7 (9)	.165
Lifetime	8 (32)	22 (28)	.801
Generalized anxiety disorder			
Current	4 (16)	11 (14)	1.00
Lifetime	9 (36)	24 (31)	.630
Alcohol dependence			
Current	4 (16)	3 (4)	.061
Lifetime	10 (40)	24 (31)	.465
Alcohol abuse			
Current	4 (16)	2 (3)	.032
Lifetime	9 (36)	17 (22)	.188
Drug dependence			
Current	2 (8)	3 (4)	.595
Lifetime	5 (20)	16 (20)	1.00
Drug abuse			
Current	2 (8)	2 (3)	.255
Lifetime	5 (20)	10 (13)	.514

[a]Two patients had lifetime but not current diagnoses available.
[b]Fisher exact test.
Abbreviation: ICG = Inventory of Complicated Grief.

ognized. Although in our sample half of the most serious suicide attempts made by CG patients occurred before the loss, data from a recently completed study of CG patients indicate a high rate of post-loss suicidality as well (K. Szanto, M.D.; M.K.S.; P. Houck, M.Stat., et al., manuscript submitted). Further prospective examination of the impact of CG on current suicidality in patients with bipolar disorder is needed.

We found greater phobic avoidance in the CG sample as measured by the Marks Fear Questionnaire, even after controlling for any current anxiety disorder and current bipolar mood state. This notable observation supports the occurrence of avoidance as a symptom of CG. Since it is difficult to measure, avoidance has been questioned as a component of CG. However, we have consistently found CG patients to engage in a range of clinically significant avoidance behaviors related to the death.

This initial survey study has several important limitations. There is the potential for ascertainment bias, with reliance on self-selection for participation and only 46.5% of patients recruited participating. We utilized self-report assessments for loss, without clinical validation. Further, we did not attempt to corroborate the reported losses in this study. It is possible that not all losses were listed and that important losses were omitted. Our data do not allow discrimination of which loss the patient had in mind when completing the ICG. Because our data are cross-sectional, we cannot confirm the direction of effect for our variables. For example, it is possible that patients with panic attacks and avoidance behaviors prior to a significant loss are at greater risk for the development and/or persistence of CG; alternately, the presence of CG may result in greater levels of panic attacks and avoidance behaviors.[26] Thus, our findings ideally should be replicated in a prospective study. Nonetheless, our results clearly indicate that researchers and clinicians working with bipolar patients need to attend to loss of a loved one and its consequences.

Complicated grief appears to occur commonly as a condition comorbid with bipolar disorder and is associated with a significantly increased risk of suicidality, high levels of anxiety and alcohol abuse, poor social support, and worsened overall functioning. There are currently no published studies documenting efficacy for pharmacologic treatment of CG. The last author's group has devised a psychosocial treatment that performed well in a pilot study[29] and in a recently completed randomized controlled trial.[28] Our observation that CG is prevalent and clinically significant in patients with bipolar disorder underscores the urgent need for work to confirm efficacious treatments for this condition.

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