Current Psychiatry Reports (2020) 22: 6
https://doi.org/10.1007/s11920-020-1130-0

BIPOLAR DISORDERS (R HIRSCHFELD, SECTION EDITOR)

Bipolar Disorder and Suicide: a Review

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Published online: 18 January 2020

Abstract

Purpose of Review Bipolar disorder has the highest rate of suicide of all psychiatric conditions and is approximately 20–30 times that of the general population. The purpose of this review is to discuss findings relevant to bipolar disorder and suicide.

Recent Findings Risk factors include male gender, living alone, divorced, no children, Caucasian, younger age (< 35 years), elderly age (> 75 years), unemployment, and a personal history of suicide attempt and family history of suicide attempt or suicide completion, as well as predominant depressive polarity. Suicide is associated with the depressed or mixed subtypes, not mania. Although there are emerging treatments for bipolar depression, such as ketamine and TMS, lithium remains the only medication associated with lowered suicide rates in bipolar disorder.

Summary Understanding clinical and demographic risk factors for suicide in bipolar disorder remains the best way to prevent suicidal behavior. Early intervention and treatment with anti-suicidal medications, such as lithium, along with close observation and follow-up is the best way to mitigate suicide in patients with bipolar disorder.

Keywords Bipolar disorder · Suicide · Suicide attempt · Suicide completion · Suicide risk factors

Introduction

Bipolar disorder is a chronic mood disorder characterized by manic or hypomanic episodes alternating or intermixed with episodes of depression [1•, 2]. The 12-month prevalence of DSM-IV bipolar disorder in the USA was estimated at 0.6%, with a lifetime prevalence of over 1% of the world's population, irrespective of nationality, ethnic origin, or socioeconomic status [3, 4]. The total prevalence of bipolar disorder could be as high as 5% if bipolar II and cyclothymia are included [5, 6]. Bipolar disorder tends to affect men more than women, with a lifetime male-to-female prevalence ratio of 1.1:1 [4]. The strongest and most consistent risk factor for bipolar disorder is having a positive family history of bipolar disorder, increasing in magnitude with degree of kinship.

Bipolar disorder is a lifelong episodic illness with a variable course that can lead to functional, occupational, and cognitive impairments [1•, 7, 8]. There are significant costs associated with this disorder, which include the direct costs of treatment, and the much greater indirect costs of decreased productivity, excess unemployment, and excess mortality [9]. The high rates of mortality are due to natural causes such as cardiovascular disease and diabetes, as well as suicide, which is a key contributor to the high mortality rate. Quality of life is also markedly impaired in patients with bipolar disorder, even when clinically euthymic, and especially with a history of previous suicide attempt [10•, 11–13].

Both DSM-5 and the International Classification of Diseases (ICD-10) [14] recognize bipolar 1 and bipolar II disorders. For bipolar I disorder, at least one manic episode must have occurred, and, although major depressive episodes are typical, they are not required for the diagnosis. For bipolar II disorder, at least one hypomanic episode and one major depressive episode are required for the diagnosis [2]. Only 20% of patients with bipolar disorder having a major depressive episode are diagnosed with bipolar disorder within the first year of treatment, and the mean delay of diagnosis is 5–10 years from illness onset [15, 16].

Patients with mood disorders are at very high risk of death by suicide compared to the general population. Patients with

This article is part of the Topical Collection on *Bipolar Disorders*

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bipolar disorder are at an even greater risk of suicide, with and approximately 20–30-fold increase than the general population.

Suicide in the General Population

Worldwide, about 800,000 to 1 million deaths per year are due to suicide [17], and it is estimated that 1.5 million will die from suicide in 2020. In developed countries, this equates to a suicide rate of 0.014% ± 0.007% per year [14/100000 person per year ± standard deviation (SD)] in general populations (Table 1) [18–24]. Suicide is a tremendous challenge for healthcare professionals and society at large. It is one of the top 10 leading causes of death worldwide, and in certain countries is the second leading cause of death in the 15–34 age group [18]. There are many risk factors for suicide in the general population and for mood disorders in particular. However, disease-specific risk factors for bipolar disorder have been more difficult to identify. Over the past few decades, studies investigating suicide risk factors in bipolar disorder have had mixed results. Risk factors for suicide in the general population include (1) male gender, (2) living alone, (3) divorced, (4) no children, (5) Caucasian, (6) younger age (< 35 years), (7) elderly age (> 75 years), and (8) unemployment [25]. Understanding the risk factors for suicide in bipolar disorder is essential for treatment planning, risk mitigation, prognosis, clinical research, and drug development.

Bipolar Disorder and Suicide

Bipolar disorder carries the highest risk of suicide compared to all other psychiatric illnesses [10•, 26–33]. However, suicide rates in bipolar disorder have been reported inconsistently when considering bipolar subtypes, gender, age, or illness severity. Although studies have differed on the relative rates of suicide in bipolar disorder patients compared to the general population, it is estimated that the annual risk of attempts is 400–1400/100,000, or approximately 0.9%, which equates to a 30- to 60-fold higher risk than the general population (Table 1) [23, 24]. In other words, about one-third to one-half of bipolar patients attempt suicide at least once in their lifetime and approximately 15–20% die due to suicide [5, 24, 34]. Bipolar disorder patients with prior suicide attempts also have a worse quality of life than bipolar patients without prior attempts [11].

The Bipolar Suicide

Clinical Features

Suicide risk in bipolar disorder varies depending on illness characteristics and phase of illness. Suicide attempts are much more common at the onset of illness during the first depressive episode and early in the course of illness rather than later on [24, 35]. Suicidal behavior is primarily associated with depressed and mixed phases of illness. Major depressive episodes are associated with the highest risk of suicide, followed by mixed episodes, and finally manic episodes, which are associated with the lowest risk of suicide. Patients with rapid cycling bipolar disorder are also at a higher risk compared to non-rapid cyclers. Suicide risk increases among bipolar patients with a longer duration of illness, and a longer duration of untreated illness. This finding is attributed to a higher frequency and duration of depression [36].

Bipolar disorder patients spend approximately half of their life symptomatic, mostly with depressed episodes or subsyndromal depressive symptoms, thereby increasing the risk of suicide. The predominant polarity of illness can be used to predict suicidal risk, with predominant-depression carrying the highest risk of suicide [5, 37–40]. Mixed-states with predominant depression also have a markedly increased association with suicide [5]. The predominant polarity of the initial episode of bipolar disorder can also be used to predict the polarity of subsequent episodes. It has been previously suggested that using the predominant polarity can be useful for the selection of appropriate maintenance treatment with either antidepressants and/or mood stabilizers for depression, or mood stabilizers and/or antipsychotics for mania [41, 42]. However, there are major limitations to this approach. Baldessarini et al. [5] showed that upwards of 47% of patients with bipolar I disorder could not be characterized by predominant polarity, which significantly limits the utility of this concept. In addition, an individual patient's classification may

Table 1 Rates of suicide

Disorder	Attempted suicide	Completed suicide
General worldwide population	0.7 to 5% per year	0.0036 to 0.037% per year
	0.8 to 2.7% lifetime prevalence	Unknown lifetime prevalence
MDD	8% per year	0.04% per year
	31% lifetime prevalence	10–15% lifetime prevalence
Bipolar I disorder	15% per year	0.4 to 0.9% per year
	33.9% lifetime prevalence	15–20% lifetime prevalence

change over time, further complicating predictive validity and clinical utility [38••, 43]. Research is unclear on whether bipolar I disorder or bipolar II disorder has the higher rate of suicide [1•, 44, 45].

Many would argue that bipolar disorder remains underrecognized and underdiagnosed, contributing to undertreatment [24]. Subsequently, more than half of bipolar patients who complete suicide were not receiving treatment at the time of their death. Furthermore, the suicide attempts of bipolar disorder patients have higher lethality than any other psychiatric disorder [46]. The proportion of suicide attempts to completed suicide in bipolar disorder is 3:1, compared to 35:1 in the general population [26]. So, not only do bipolar patients carry a much greater burden of depression compared to other psychiatric disorders, they make more lethal attempts, which contribute significantly to the high rate of suicide completion.

Studies of Suicide Risk Factors in Bipolar Disorder

While the general suicide risk factors also apply to bipolar patients, there are some distinct disease-specific risk factors as well, defining these risk factors has been difficult (Table 2). Over the past few decades, studies investigating the risk factors for suicide in bipolar disorder have varied greatly in study design, changes in diagnostic criteria, and diagnostic switching. Moreover, assessing suicide requires a lot of effort with large samples, and the majority of persons will not commit suicide, even among patients with prior attempts. For that reason, suicide is a rare event, and, historically, investigating rare events within any population is problematic. Even a small change in the demographic variables in a sample from one study to the next can lead to conflicting results.

Gender, history of suicide attempt, suicidal ideation, family history of suicide, mood episodes, rapid cycling illness, age of

Table 2 Suicide risk factors in bipolar disorder

Sociodemographic factors	• Men have higher rates of completed suicide
	• Women have higher rates of attempted suicide
	• Caucasian
	• Marital status (single, widowed, divorced)
	• Living alone
	• No children
	• Younger age (< 35 years), elderly age (> 75 years)
	• Unemployment
Clinical history	• History of prior suicide attempt(s)
	• Family history of attempted or completed suicide(s)
	• Suicidal ideation
	• Predominant depressive polarity
	• Major depressive episode
	• Phase of illness: depression > mixed > dysphoric mania > pure mania > euthymia
	• Rapid cycling subtype
	• Earlier age of onset
	• Earlier stage of illness course
	• Longer duration of untreated illness
	• Number of previous depressive episodes
	• Previous hospitalization(s)
	• Concurrent medical comorbidity
	• Mood-incongruent psychotic symptoms
Psychiatric comorbidity	• Personality disorders: borderline, antisocial, histrionic, narcissistic
Genetic factors	• Noncoding RNA *LOC105374524*
	• Serotonin-related genes: *5-HTT*, *5-HT1–7*, *TPH1*, *TPH2*
	• Other genes: *AKT1*, *AKT1P*, *ADRA2*, BDNF, *COMT*, *CREB1*, *GSK3B*, *FOX03A*, and *MAPK1*
Other (needs further study)	• Alcohol and drug use disorders
	• Childhood abuse and neglect
	• Aggressive or impulsive behavior
	• Higher altitude
	• Dysfunctional personality traits
	• Poor social support

onset, episode polarity, polarity of first affective episode, history of trauma, drug abuse, personality disorders, and personality features, have all been studied as risk factors for suicide in bipolar disorder (Table 2) [24, 47•]. Conflicting results for gender as a risk factor in bipolar disorder are common. Some studies have shown that men tend to have higher rates of completed suicide, while women have higher rates of suicide attempts, especially at younger ages, indicating higher lethality of suicidal acts in men [48–50]. Other studies have found no gender difference in suicide attempts [51]. Although many studies have demonstrated that males have a higher rate of suicide, often using more violent means, there remains no clear difference between males and females [34, 49, 52–54].

One of the most robust predictors of suicide attempts and suicide completions in patients with bipolar disorder is a history of prior suicide attempts [24, 50, 53–56]. Prior suicide attempt increases the risk of completed suicide by 37-fold in bipolar patients [57], and at least half of suicides occur in individuals with prior attempts [46, 58]. Suicidal ideation has been associated with subsequent suicides and suicide attempts among bipolar disorder patients. Suicidal ideation itself varies from 14 to 59%, and is related to hopelessness, mixed depression, severe depression, psychotic symptoms, past suicide attempt, alcohol abuse, panic disorder symptoms, and earlier age of onset [24, 59, 60]. Suicidal ideation occurs in 79% of bipolar patients during the depressed phase, and is also significantly associated with mixed phases, both of which have a much stronger association than during mania [24, 61]. In bipolar disorder, a positive family history of attempted and completed suicide increase risk for suicide, especially in first-degree relatives [53, 54]. This is partly explained by the heritability of bipolar disorder itself (40%), as well as familial transmission of suicidal behavior [62].

Major depressive episodes alone are a significant risk factor for suicide in bipolar disorder, with the majority of attempted and completed suicides occurring during depressive phases. In addition, if the first mood episode has a predominant-depressive polarity, there is an eightfold greater risk for suicide attempt. Predominant-depressive polarity in subsequent episodes is associated with increased risk of suicidal acts and suicide attempts [5, 39, 41, 63]. Suicidal ideation and behavior is also relatively common in mixed episodes and dysphoric mania, with 26–55% of patients with dysphoric mania having suicidal ideation, and only 2–7% in patients with pure mania [24, 35, 52]. However, bipolar disorder patients attempt or commit suicide mostly during severe, pure, or mixed depressive episodes (78–80%), much less frequently during mixed affective episodes or dysphoric mania (11–20%), and very rarely during states of euphoric mania or euthymia (0–7%) [24, 64]. Severe, agitated and/or anxious major depression, especially with recurrent insomnia in the presence of a past suicide attempt is associated with the highest-risk for suicide in bipolar patients [24, 65]. The rapid cycling subtype of bipolar disorder has also been identified as a risk factor for suicide attempts, with a 54% higher risk for attempted suicide, and higher intent and lethality compared to non-rapid cyclers [54, 66]. Other characteristics of the mood disorders have been associated with suicide, including an increased risk at the onset of illness during the first depressive episode, earlier stage in the illness course, longer duration of untreated illness, number of previous depressive episodes, previous hospitalizations, and concurrent medical comorbidity [28]. There is also an association with emergence of mood-incongruent psychotic symptoms and increased suicidal risk [67].

Age of onset of bipolar disorder has been associated with the risk for suicide attempt, with younger age at diagnosis associated with a higher risk [49, 54]. There is inconclusive evidence for the traditional alcohol and drug use disorders and nicotine use disorder as risk factors for suicide in bipolar disorder. Suicide risk is significantly increased with comorbid personality disorders, including the borderline, antisocial, histrionic, and narcissistic types. These personality disorders are associated with higher rates of severe mood episodes, environmental reactivity, and increased impulsivity, and aggressiveness [24]. Other risk factors, which have not been thoroughly studied, and likely contribute to suicidality, include childhood abuse and neglect [28], higher altitude [68•], dysfunctional personality traits[69, 70], marital status (single, widowed, divorced), poor social support, spirituality, and religiosity [10·]. Overall, the most consistent and robust risk factors for suicide in bipolar disorder across studies are a personal history of attempted suicide and a family history of attempted or completed suicide.

Assessment of the Suicidal Bipolar Patient

Clinical assessment of the suicidal bipolar patient should always be carried out at the earliest possible opportunity with direct clinical inquiry. There are general risk assessment tools that may allow physicians to identify high-risk patients and initiate treatments early and effectively (e.g., the Columbia-Suicide Severity Rating Scale (C-SSRS) [71], Columbia Classification Algorithm of Suicide Assessment (C-CASA) [72], The Tool for Assessment of Suicide Risk (TASR) [73], the Oxford Mental Illness and Suicide tool (OxMIS) [74], or the Modular Assessment of Risk for Imminent Suicide (MARIS) [75]). However, these tools should never be used as a replacement for thorough clinical assessment, even though there are no clearly defined criteria have been established to predict suicide risk in an individual patient. Currently, there are no validated suicide risk assessment tools specifically for bipolar disorder.

Suicide assessment should include a thorough psychiatric examination of mental status, focusing on mood, irritability,

the presence or absence of psychosis, and suicidal ideation and plans. Special attention is required to establish the nature, extent, and duration of suicidal ideation, and whether the patient has a plan; the method they intend to use; and the extent, nature, and lethality of previous suicide attempts; as well as the patient's access to lethal means [76]. In addition, investigation into the nature of the patient's affective temperament (depressive, cyclothymic, hyperthymic, irritable, and anxious) and personality traits could more clearly establish suicide risk [49]. Establishing possible protective factors, such as marriage, children, employment, and religious beliefs, can be equally as important as establishing risk factors. The patient's history of medication and treatment adherence will also contribute to treatment planning. The involvement of family members and/or close friends should be included as informants during the initial evaluation (providing consent has been obtained) to gather additional information and to prepare for treatment planning and follow-up care. If believed to pose a risk to him- or herself, the patient should be hospitalized.

For patients with an elevated risk of suicide treated on an outpatient basis, follow-up assessments should occur at regular intervals after the initial assessment, paying close attention to any change in clinical status and emergence of new symptoms (i.e., mixed episode). Patients with suicidal thoughts have typically had thoughts of suicide for a long period of time, and most patients are willing to discuss these openly. Therefore, the clinician should not avoid discussing suicide out of fear of provoking suicidal behavior or personal discomfort with the topic. This is an important issue that needs to be addressed with all patients, especially those with significant risk factors.

It is notable that a large proportion of individuals (regardless of diagnosis) who eventually complete suicide will have made contact with mental health services in the months preceding their death [26]. The risk of suicide is elevated in the first several weeks after discharge from a psychiatric hospital [77]. It has been estimated that as much as 75–83% of individuals who completed suicide had been in contact with a physician within the previous 1 year. Additionally, only 46% had seen a mental health professional within a month and 36% in the week before death. This makes the detection of individuals at acute risk for suicide extremely difficult, and suggests that effective interventions for many, and perhaps most, suicidal patients may not occur.

Management of the Suicidal Bipolar Patient

Bipolar patients brought into the emergency department after suicidal threats or non-harmful attempts present one of the greatest challenges to psychiatrists. Conservatively, the best course of management is to admit such patients to a psychiatric inpatient unit for protection and treatment. In general, any patient with suicidal ideation or attempt and depression who is psychotic, intoxicated, cannot attend to daily needs, or whose well-being is in doubt by the clinician should be admitted for observation and treatment. In some cases, a court order will be needed to hospitalize the patient.

Pharmacotherapy

The first step in the management of bipolar disorder is to confirm the diagnosis, because the therapeutic approach differs depending on the phase of illness. In general, mood stabilizers and antipsychotics are the mainstay of acute management of mania and depression [1, 49, 78]. Lithium has long been known to reduce rates of suicide attempts and completions in depressed and bipolar patients. Multiple randomized controlled trials and meta-analyses, as well as decades of clinical experience, have shown that lithium significantly reduces the risk of self-harm and suicide in unipolar depression and bipolar depression [25, 79–82]. In one study of 50,000 bipolar patients, lithium was found to reduce the rate of completed suicide and other suicide-related events by 14% relative to treatment with valproate [81••]. However, lithium is not an acute intervention, rather a prophylaxis against suicide, and can be lethal in overdose. Long-term lithium use decreases the risk of death by 60–80% [80, 83]. Lithium non-adherence increases suicidal risk, and lithium discontinuation increases the risk of death by 13-fold [63, 84]. A more rapid treatment of suicidality is possible with intravenous and intranasal ketamine for bipolar patients [85–87], but ketamine is not widely available.

As for other mood stabilizers, after investigating 199 clinical trials of 11 antiepileptic drugs (AEDs; carbamazepine, divalproex, felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, pregabalin, tiagabine, topiramate, and zonisamide) for three different indications, including epilepsy, pain, bipolar disorder, and other psychiatric disorders, the Food and Drug Administration (FDA) has reported that there is an increased risk of suicide. However, this report has been thoroughly questioned over the last decade, and studies have shown that AEDs do not increase the risk of suicide attempts or completed suicide in patients with bipolar disorder [88, 89]. Moreover, valproate, lamotrigine, and carbamazepine have been shown to have a possible anti-suicidal effect, although less than what is reported for lithium [55, 90, 91].

Although antidepressants significantly reduce the risk of suicide in depressed patients with long-term treatment, no antidepressant medication has demonstrated an anti-suicidal effect [77, 92]. In fact, some studies have suggested that antidepressant treatment might increase suicidality in a subgroup of bipolar patients, which has not been shown for completed suicides [28]. There also remains a concern that antidepressant medications can worsen the course of disease by provoking a switch into a hypomanic, manic, or mixed mood state, or

inducing agitation in mixed episodes, possibly contributing to suicidal behavior [93]. However, the International Society for Bipolar Disorders (ISBD) task force acknowledged that some bipolar patients might benefit from antidepressant medication, with bupropion having the lowest risk of switching, only as long as they are prescribed as an adjunct to mood stabilizers [94].

Quetiapine, lurasidone, and olanzapine/fluoxetine are the antipsychotic medications of choice for treatment of bipolar depression. Some atypical antipsychotics (aripiprazole, olanzapine, and quetiapine) may have an acute antidepressant effect and long-term mood-stabilizing effect in patients with bipolar disorder, but there is no specific evidence for an anti-suicidal effect [26, 95]. Clozapine is the only antipsychotic medication that has FDA approved for use in the reduction of recurrent suicidal behavior. However, this is limited only to patients with schizophrenia or schizoaffective disorder, and there is currently no indication for its use in bipolar disorder. In addition, current evidence suggests that antipsychotic medications should only be used in addition to mood stabilizers for breakthrough hypomanic or manic episodes, and discontinued as soon as clinically feasible due to the long-term metabolic side effects [96].

Electroconvulsive therapy (ECT) is effective in eliminating acute suicidal risk in severely depressed and deeply suicidal adult patients [83, 97, 98]. ECT has also been considered as the treatment of choice in emergency situations for patients with high suicide risk [99]. Compared with current pharmacotherapy treatments, ECT has superior anti-suicidal effects in patients with both unipolar and bipolar depression [100]. However, the long-term effect of ECT for the treatment of suicidality in patients with bipolar disorder is unknown [49, 101].

Transcranial magnetic stimulation (TMS) and repetitive TMS (rTMS) are both approved as therapy for treatment-resistant major depressive disorder, with a possible short-term decrease in suicide risk. Although studies have shown a potential benefit from the use of TMS and rTMS in bipolar depression, there remains a theoretical risk of switching to hypomania or mania, and TMS is not currently approved by the FDA for bipolar depression [102–104].

Vagal nerve stimulation (VNS) is approved as adjunctive therapy for treatment-resistant major depressive disorder, but only if the patient has failed 4 or more different medications [105]. There is little evidence for the use of VNS in bipolar depression, and it is not currently FDA approved for this indication.

Psychotherapy

While the efficacy of dialectical behavioral therapy in reducing the frequency of suicide attempts and deliberate self-harm has been shown in several studies in patients with borderline personality disorder [83, 106, 107], the modality has not been used in patients with bipolar disorder. In general, psychotherapy and other psychological treatments are used as adjuncts to pharmacotherapy in the treatment of suicidal patients [83, 108]. However, only a small number of studies have investigated psychological treatment for suicidality in bipolar disorder, and no clear benefit has been shown [26, 83, 108].

Prediction and Prevention of Suicide in the Bipolar Patient

The natural history of bipolar disorder often includes periods of remission; however, recurrence is common in bipolar patients, particularly with poor treatment adherence. Predicting recurrent episodes is extremely difficult, and there are currently no validated clinical or biological measures that can be used in patients with bipolar disorder.

Genetics

The ultimate goal of genetic studies on suicide is to translate underlying biological mechanisms into treatments and prevention strategies. Genetic risk factors have been consistently found to play a significant role in suicide in bipolar disorder, as demonstrated by primary studies and also supported by twin, family and adoption studies [44, 46, 47•, 67]. Candidate gene studies have found evidence for the role of genetic variation in suicidality, but many of these studies have had mixed results [26]. Serotonin-related genes (transporters and receptors), such as *5-HTT* and *5-HT1–7*, and tryptophan hydroxylase genes, *TPH1* and *TPH2*, have shown a significant association with the risk of suicidal behavior. Many other genes, such as *AKT1*, *AKT1P*, *ADRA2*, BDNF, *COMT*, *CREB1*, *GSK3B*, *FOX03A*, and *MAPK1*, have all been associated with suicidal behavior [26, 109–111]. Most recently, the largest genome-wide association study (GWAS) to date, found 3 genome-wide significant loci for increased risk of suicide attempt: one for major depressive disorder, one for bipolar disorder, and one for mood disorders [112]. For bipolar disorder, this was an insertion-deletion polymorphism on chromosome 4, an intronic variant in the noncoding RNA *LOC105374524*.

Neuroimaging

There is some evidence to suggest that white matter hyperintensities (WMH) in the brain of patients with bipolar disorder may increase suicidal risk [113–116]. However, these results could be obscured by the correlation between increased WMH volume in relation to the diagnosis of bipolar disorder itself, and associated with disease burden, not directly related to the degree of suicidal risk [117].

Endocrinology

Altered functioning of the hypothalamic-pituitary-adrenal (HPA) axis has been reported in suicidal behavior in bipolar disorder [118]. However, many studies of HPA axis function in bipolar disorder have not specifically examined the potential effects of suicidal behavior, and studies showing an association between HPA axis activity and suicidality have been mixed [119–121]. There is also no current clinical indication for the benefit of measuring salivary/plasma cortisol levels or performing a dexamethasone suppression test in patients with bipolar disorder to assess suicidal risk.

Conclusion

Bipolar disorder carries a high burden of disability and has the highest risk of death by suicide compared with other psychiatric disorders. Suicide is difficult to predict, but certain risk factors, including history of past suicide attempt, and family history of suicide attempt or suicide completion, as well as a predominant depressive polarity, can be used to assess risk in patients with bipolar disorder. Early intervention and treatment of bipolar depression with mood stabilizers and/or antipsychotics, along with close observation and follow-up is the most effective way to mitigate suicide in these patients. Lithium may offer an advantage of lowering the patient's risk for suicidal behavior. ECT could also provide a fast and effective means of treating suicidality in bipolar disorder. Close involvement of family members or friends, a supportive social environment, as well as psychological support can provide further benefit. There are currently no validated genetic, neuroimaging, or clinical biomarkers that can be used for the assessment of suicide risk.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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