

## Research report

# STRESSFUL LIFE EVENTS AND OTHER ASSOCIATED FACTORS IN PATIENTS WITH BIPOLAR DISORDER CURRENT EPISODE DEPRESSION – A CROSS-SECTIONAL STUDY

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### ABSTRACT

**Background:** Bipolar disorder (BD) is a mental illness which leads to considerable difficulties and challenges. The neurobiology of BD has complex underpinnings of gene–environment interactions. One such environmental factor, stressful life events (SLEs) can have adverse impacts on the course and prognosis of BD, however, this is underexplored. **Aims and objectives:** 1) To estimate the frequency and severity of SLEs in patients with BD-current episode depression 2) To determine the association of severity of depression with SLE, sociodemographic and illness-related factors. **Methods:** This was a cross-sectional study done on 100 consecutive patients diagnosed to have BD-current episode of depression (ICD-10), attending Psychiatry department at Pushpagiri Medical College, Thiruvalla, Kerala. A semi-structured proforma, Hamilton Rating Scale for Depression, Presumptive Stressful Life Events Scale and Brief Psychiatric Rating Scale were used. **Results:** About 73% of patients reported SLEs – of which 65% had mild/moderate and 8% had severe stress. A statistically significant association was found between SLEs and ‘very severe’ depressive episode. Past suicide attempt, the first episode as depression and lesser duration of the last episode also showed a statistically significant association with severity of depression. **Conclusion:** As the stressful life experiences have been linked to ‘very severe’ depressive episodes in a major way, understanding the association of stressful life events and BD can help in predicting further relapses and complications like suicide. It can aid in both symptom reduction and improving quality of life as well.

**Key words:** Stressful life events, bipolar disorder, depression.

### INTRODUCTION

Bipolar disorder (BD) is a severe, recurrent affective disorder, with episodes of hypomania/mania and depression which are interspersed with periods of euthymia.<sup>1</sup> Bipolar disorder accounted for 9.9 million DALYs in 2013, explaining 0.4% of total DALYs and 1.3%

of total YLDs. There were 5.5 million DALYs recorded for females and 4.4 million for males.<sup>2</sup> The course is chronic with impairment in the functioning of affected individuals and it carries a significantly elevated morbidity and mortality risk.<sup>3</sup> The International Classification of Diseases – Eleventh Edition (ICD-11) subdivides bipolar disorder into type I (mania

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and depression) and type II (hypomania and depression) disorders.<sup>4</sup> Females have a greater risk for mood disorders than males; however, the prevalence of bipolar disorder is almost equal in both sexes.<sup>5</sup>

There is compelling evidence that genetic risk factors have a role in the onset and progression of this condition. According to epigenetic studies, early-life events increase genetic vulnerability, which later acts as a major determinant for the disease's first clinical manifestations.<sup>6</sup> In addition to the genetic/biological factors, psychosocial factors also influence the onset, type, timing, and outcome of affective episodes.<sup>7</sup> The neurobiology of BD has complex underpinnings of gene-environment interactions.<sup>8</sup> One such environmental factor that affects the course of the disease irrespective of genetics is stressful life events (SLEs).<sup>9</sup> Life events are defined as discrete experiences that disrupt an individual's usual activities, causing substantial change and readjustment.<sup>10</sup> These are the significant changes in one's personal circumstances that have personal and social ramifications.<sup>11</sup> Life events might happen suddenly or in a predictable fashion. Bipolar patients with prior life events take threefold more time to achieve recovery when compared to others.<sup>12</sup> The prevalence of SLEs in patients with BD is higher than that in healthy individuals.<sup>13</sup> SLEs have been found to be associated with the initiation of manic episodes, depressive episodes, earlier episodes, and early onset of illness in bipolar patients.<sup>13</sup> The quality of the patient's family or psychosocial environment has been speculated to be a potentially crucial intervening variable in prior attempts to establish environmental factors that affect the onset, course, and resolution of bipolar illness.<sup>14</sup>

However, data is contradictory in terms of the effect of life events on relapses: Some retrospective and prospective studies proposed a negative impact on the course of bipolar patients, especially on depressive episodes.<sup>15,16</sup> Also, the time frame for SLEs causing a relapse

of an episode of BD has been proposed to be four weeks for manic and six months for depressive episodes. The presence of a stressor predicted a longer time to functional recovery in life domains: up to 112 days in work/school in bipolar patients. There are several studies, on the contrary, which did not find any significant relationship between SLEs and bipolar disorder.<sup>17</sup> Despite the fact that positive studies outnumber negative studies, establishing a causal link between SLEs and BD is difficult, not only because of the methodological variability of these studies and their results but also because SLEs may be a consequence of the illness rather than the cause.<sup>18,19</sup> Individuals with BD are more likely to have SLEs prior to an episode than nonpsychiatric controls, and SLEs appear to be more prevalent before relapse in patients with BD than at other times in their lives.<sup>13</sup> Early adversity sensitization, kindling/behavioural sensitization, hypothalamo-pituitary-adrenal (HPA) axis dysfunction, neurogenic hypothesis, and social rhythm disturbance are some of the postulated reasons underlying the link between SLEs and BD.<sup>7,11,14</sup> In a study conducted by Simhandl et al. (2015), despite advances in the treatment of bipolar disorder, almost 70% of bipolar I and II patients were found to relapse within four years, with a mean of 208 days until the next affective episode. This pattern highlights the need to better understand the predictors of the course of illness, especially the psychosocial factors.<sup>20</sup>

The Indian population, which is currently undergoing fast industrialization and urbanization, is exposed to increased psychological stress from modern living, which may lead to the development of mental illnesses, such as mood disorders, among the vulnerable. There is a need for better recognition and understanding of the psychosocial components associated with BD, particularly bipolar depression, as the full impact of SLEs on the course of BD is not fully understood and only a small number of studies on the involvement of SLEs in bipolar disorder have emerged from India.

## Objectives

1) To estimate the frequency and severity of SLEs in patients with BD - current episode depression.

2) To determine the association of severity of depression with SLEs, sociodemographic factors and illness related factors.

## METHODOLOGY

A cross-sectional study was conducted in the Department of Psychiatry of a tertiary care centre in Central Kerala, India, over a period of one year from September 2020 to September 2021. Institutional ethics committee clearance for the study was obtained in November 2019.

Study tools used included a semi-structured proforma, Hamilton Rating Scale for Depression (HAMD) and Presumptive Stressful Life Events Scale (PSLES). HAMD is one of the most widely used clinician-administered depression assessment scale. It contains 17 items with emphasis on melancholic and physical symptoms of depression. Each item is scored from 0 to 4. A total score of 0-7 is considered normal, 8-13 as mild depression, 14-18 as moderate depression, 19-22 as severe depression and >23 as very severe depression. It has a sensitivity of 79% and specificity of 87%.<sup>21</sup> PSLES is standardized for Indian population. In this scale, each of the 51 different life events experienced by the population in the past one year is given mean stress score. A total score of <40 suggests that there is no stress, 40-200 less or moderate stress and >200 severe stress.<sup>22</sup>

Individuals of both genders, diagnosed with BPAD – current depressive episode according to ICD-10, aged 18 to 65 years, accompanied by a key informant whose information was reliable and adequate and had a duration of illness of at least two years were included in the study. The participants were selected after obtaining informed consent. Individuals with intellectual disability and organic mood disorders were excluded from the study. Sample size was calculated by taking the proportion of stressful life events among BD patients as 69.5%, type I

error as 5% and absolute precision as 10% to be 100.<sup>27</sup>

A semi-structured proforma was used to collect sociodemographic details and illness related factors by interview method by the principal investigator. Severity of the current depressive episode was assessed using HAMD and PSLES was used to assess the presence of a stressful life event that had occurred in the last one year.

The data was analyzed using SPSS version-20 and is presented as frequency and percentage of patients with stressful life events. The clinical and sociodemographic variables are presented as frequency and percentage for categorical data and mean and standard deviation (SD) for continuous data. The association between the severity of depression and these factors was assessed using the Chi-square test. A p-value of less than 0.05 was considered to be statistically significant.

## RESULTS:

The mean age of the participants in this study was 44.74 years (SD – 14.624). The majority were females (52%), between the ages of 31 and 60 years (54%), were married (64%), and practised Christianity (55%). All participants were literate, with the majority having completed secondary school (39%). It was found that 36% of the study participants were housewives, 20% were unemployed, and 13% were non-professional workers. Semi-urban areas supplied 48% of the study population, while rural and urban areas contributed 34% and 18%, respectively. The majority of the study participants were from nuclear, middle-class families with a monthly family income of Rs 20,000 - Rs 30,000 (See Table 1). Stressful life events were experienced by 73% of the study participants.

When the illness-related factors are taken into account, the majority of the research participants were between the ages of 20 and 30 years when they had their first episode. Only 4% of the population had an age of onset of more than 50 years. The majority of the

Table 1. Distribution of study sample based on socio-demographic variables

Variable	Frequency (%) (N=100)
<i>Age</i>	
18-30 years	24 (24.0)
31-45 years	27 (27.0)
45-60 years	27 (27.0)
61-75 years	22 (22.0)
<i>Sex</i>	
Male	48 (48.0)
Female	52 (52.0)
<i>Religion</i>	
Hindu	34 (34.0)
Muslim	11 (11.0)
Christian	55 (55.0)
<i>Education</i>	
Primary	13 (13.0)
Secondary	39 (39.0)
Diploma	24 (24.0)
Degree	24 (24.0)
<i>Occupation</i>	
Laborer	8 (8.0)
Non professional	13 (13.0)
Professional	9 (9.0)
Housewife	36 (36.0)
Student	3 (3.0)
Retired	11 (11.0)
Unemployed	20 (20.0)
<i>Income</i>	
Rs.1000-10,000/-	2 (2.0)
Rs.10,000-20,000	20 (20.0)
Rs.20,000-30,000	28 (28.0)
Rs.30,000-40,000	15 (15.0)
Rs.40,000-50,000	18 (18.0)
Rs.>50,000/-	17 (17.0)

participants in the study had a total duration of illness of more than 25 years (26%). In their lifespan, the majority of the study participants (45%) had 5-10 episodes of mania or depression. In the current depressive episode of BD, 43% of the study sample exhibited concomitant psychotic symptoms and 45% of the participants experienced suicidal ideation. Mania was the first episode in 51% of the research participants. A family history of mental illness, including suicide, was found in the majority of the study participants (64%).

Diabetic or hypertensive patients constituted 26% of the study sample. History of coronary artery disease and cerebrovascular accidents were found in 2% and 4% of the sample, respectively. Hypothyroidism affected 14% of the participants, while 10% had a history of alcohol abuse in a dependent pattern and 14% had tobacco dependence. Cannabis was abused by 4% of the study participants.

Stressful life events in the past year were communicated by 73% of the study subjects – 8% of the individuals reported severe stress and 65% mild to moderate stress (see Figure 1). No stressful life events were identified in 27% of the study sample. The mean score of HAMD was 22.27 (SD – 6.23). Very severe depression was observed in 43% of the participants (see Figure 2). A statistically significant association was found between stressful life events and ‘very severe’ depression ( $p = 0.004$ ) (see Table 2). Other factors that were found to have a statistically significant association with the severity of depression were (see Figures 3 & 4):

- Past suicide attempt ( $p = 0.03$ )
- First episode being depression. ( $p = 0.03$ )
- Duration of last episode. ( $p = 0.024$ )

## DISCUSSION:

Bipolar disorders are characterized by repeated (at least two) episodes in which the mood and activity levels are significantly disturbed. The episodes may be manic, depressive or mixed episodes.<sup>23</sup> In this study, severity of the current depressive episode was assessed using HAMD. PSLES was used to assess the presence and severity of stressful life events.

The mean age of the participants was 44.74 years (SD – 14.624) and the majority were females. This was consistent with the study by Tsuchiya et al. (2003), where the prevalence of bipolar was found to be almost equal between males and females.<sup>24</sup> All individuals in the study sample were literate. The overall educational status of the study population was high when compared to other parts of India. This could be

Table 2. Association between severity of depression & illness-related factors

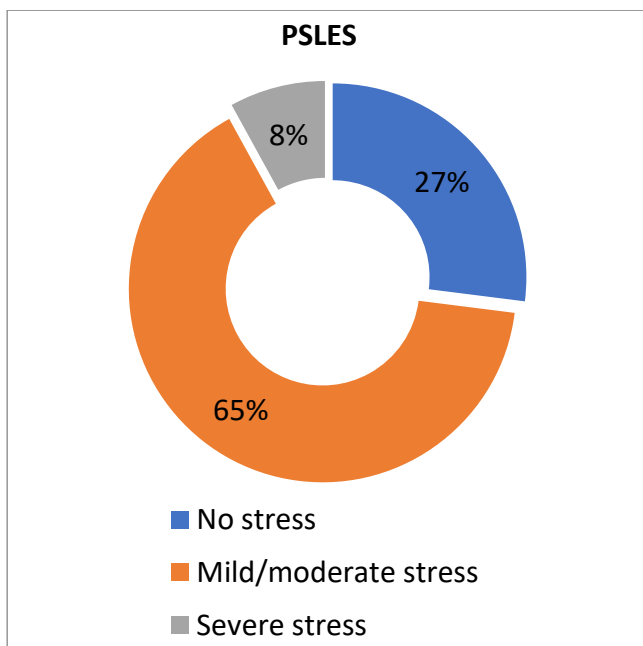
Illness related factors		Severity of depression F (%)			χ <sup>2</sup> /FE test (p-value)
		Moderate	Severe	Very severe	
*Duration of the last episode	2-4 weeks	3 (27.3)	0 (0.0)	8 (72.7)	†(0.024)
	1-2 months	8 (34.8)	12 (52.2)	3 (13.0)	
	2-4 months	9 (27.3)	8 (24.2)	16 (48.5)	
	4-6 months	6 (26.1)	6 (26.1)	11 (47.8)	
	>6months	2 (20.0)	3 (30.0)	5 (50.0)	
*Past suicide attempt	Yes	4 (15.4)	5 (19.2)	17 (65.4)	7.25 (0.03)
	No	24 (32.4)	24 (32.4)	26 (35.1)	
*Presence of stressful life events	Present	17 (21.8)	21 (26.9)	40 (51.3)	11.06 (0.004)
	Absent	11 (50.0)	8 (36.4)	3 (13.6)	
*First episode	Depression	13 (26.5)	9 (18.4)	27 (55.1)	7.09 (0.03)
	Mania	15 (29.4)	20 (39.2)	16 (31.4)	

\* - p value < 0.05, † - Fisher’s exact test

due to the higher literacy rates in Kerala state. The findings were similar to the study by Pradip et al. (2019), where 34% of the individuals in the study group had secondary level of education, 26% had higher secondary level of education and 40% were graduates.<sup>25</sup> Among the study participants, the majority of the subjects practised Christianity, which could be in accordance with their place of residence as well as due to the institution being a Christian mission hospital situated in a Christian-

majority area. In this study, the majority of the participants came from semi-urban or rural areas of Kerala. This is in accordance with the Census Report 2011, which shows that the majority of the people in Kerala belonged to rural or semi-urban areas.<sup>26</sup> In the study, the majority of the participants belonged to nuclear type of families. This vividly demonstrates the impact of urbanisation and migration, resulting in the required fragmentation of the traditional Indian joined family system.

Figure 1. Severity of stressful life events according to PSLES scores



According to the present study, about 73% of patients reported SLEs – of which 65% had mild/moderate stress and 8% had severe stress. In the study conducted by Sam et al. (2019), about 69.5% of the relapsed BD patients had SLEs in the pre-onset period. About 72.6% of the relapsed males reported pre-onset SLEs versus 65.5% of the relapsed females.<sup>27</sup> Similar results were obtained in the study conducted by Koenders et al. (2014), where negative life events were significantly associated with subsequent depressive mood and depression-dependent functional impairment.<sup>28</sup> When severe negative life events occur, they appear to trigger an increase in bipolar depression.<sup>29</sup>

In contrast to another study where there was a significant association between sociodemographic factors and severity of the depressive episode, in the present study, the sociodemographic details were not found to

Figure 2. Distribution of the sample (in %) according to the severity of depression based on HAMD scores

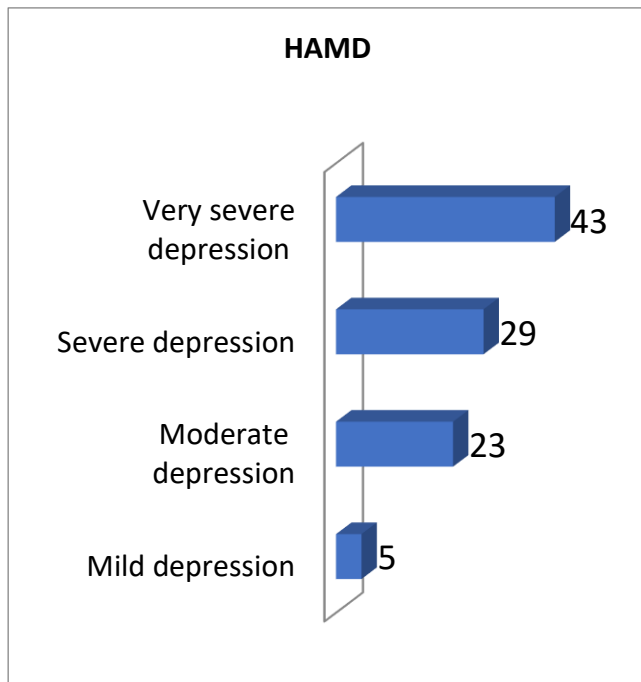
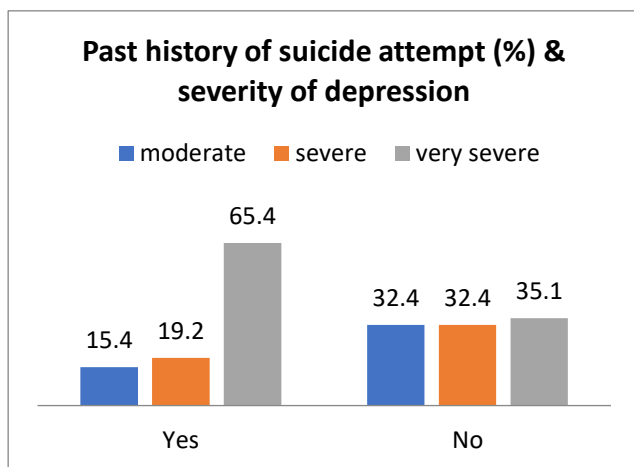


Figure 3. Association of past history of suicide attempt and severity of depression



have any significant association with the severity of depression.<sup>24</sup>

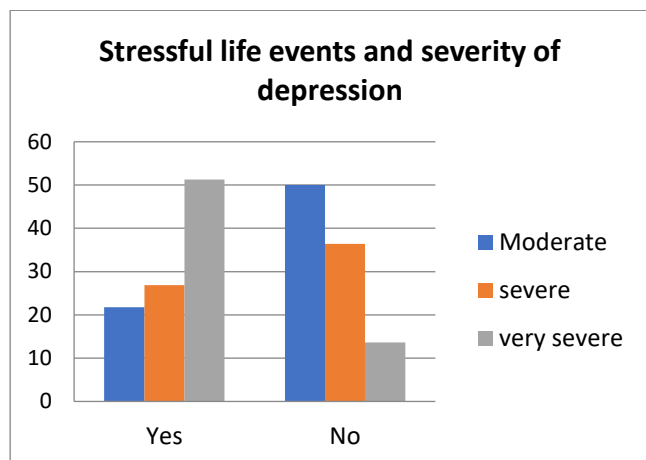
No association was found for the severity of depression with substance abuse and medical comorbidities. However, other studies showed a significant link between alcohol/substance abuse and relapse as well as increased severity of the episode.<sup>30</sup> Medical comorbidities were also revealed to be determinant in the severity of the present episode in other studies.<sup>31,32</sup>

Among the illness-related factors, a statistically significant association was found between the severity of depression and stressful life events, a less-than-one-month duration of the previous episode, presence of suicide attempt in the previous episode and the first episode being depression. This was similar to the findings from another study which found that patients experience more life events prior to relapses into either manic or depressive episodes than during euthymic periods.<sup>33</sup> They also experienced more life events relative to healthy individuals and physically ill patients. Other studies also reported a rather stable and high prevalence of SLEs during the pre-onset period of relapse.<sup>27</sup> This association shows that in bipolar disorder, a thorough history taking including the details about the previous episodes, is necessary for understanding the course and progression of the illness. It will also help the clinician choose the treatment plan and setting. A detailed assessment of the presence of the precipitating, perpetuating, or predisposing factors is important since resolving these issues could be crucial for the prognosis of the current episode and the avoidance of further ones. Also, psychosocial interventions like behavioural therapy, cognitive behavioural therapy, interpersonal psychotherapy, and problem-solving therapy could aid in a faster recovery.<sup>34</sup> Stressful life events in bipolar have also been linked to a bidirectional relationship, with evidence that they occur both before and after mood episodes.<sup>28</sup>

### Conclusion and recommendations:

SLEs are defined as discrete, quantifiable experiences that can have a significant negative impact on a person's life.<sup>35</sup> It can either precipitate an episode or worsen the course of an ongoing episode. In the present study, stressful life events prior to the episode were present for 73% of the participants. The severity of the depressive episode had a significant association with stressful life events. The presence of a prior history of suicide attempt was found to be associated with the

Figure 4. Multiple bar diagram showing the association of stressful life events (X axis) and severity of depression (Y axis)



severity of depression. Hence, these patients should be closely monitored and family members be given psychoeducation about the likelihood that the current symptom might get worse and lead to complications like suicide which can be prevented. It underlines the importance of screening for and addressing life events in bipolar patients, as possible. In a similar way, patients with their first episode of depression were found to have a severe current episode. As a result, the clinician must be aware of the likelihood that the current symptoms would worsen, and as a result, prepare the setting and the approach to treatment accordingly.

The mental health programs could also aim at identifying the stressful life events or factors that may contribute to or precipitate the illness.<sup>36</sup> The National Mental Health Survey called for a significant strengthening of the existing National and District Mental Health Programmes after noticing a huge and unmet gap in mental health services, which needs our immediate attention.<sup>37</sup> Therefore, assessing the significance of stressful life events and factors in the course and prognosis of bipolar disease, particularly depressive episodes, is critical.

#### Limitations of the study:

- Study subjects were in-patients in a tertiary

care centre; hence it would be difficult to generalize the results to the general population.

- Cross-sectional descriptive design doesn't provide any information on the course of the comorbidities, changes in the severity, causality and quality of life over time. A detailed follow-up of these patients is required, which was not included in the present study.
- Stressful life events were not individually considered.
- The time duration between the stressful life event and the onset of illness was not specifically studied.
- Frequency and duration of hospitalization, which are also taken as indirect markers of the severity of illness, were not computed in the present study.

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