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Stressful life events and social support in bipolar disorder: a cross-sectional study from South India shows a greater severity of stress in the pre-onset period as risk factors for relapse

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Abstract

Background: The full impact of stressful life events and social support in the course of bipolar disorder is poorly understood and limited relevant research is available. Consequently, we intended to determine the impact of stressful life events and social support in patients with bipolar disorder attending a tertiary care centre during a period of one year.

Methods: 157 patients with bipolar disorder either in relapse or in remission according to DSM-5 diagnostic criteria were included in the study by consecutive sampling after taking informed consent. They were assessed using a semi-structured demographic proforma, the Hamilton Depression Rating Scale, the Young Mania Rating Scale, the Presumptive Stressful Life Events Scale, and Oslo's Social Support Scale.

Results: 56.7% (89/157) of the patients had a relapse episode and 43.3% (68/157) were in remission. 75.3% (67/89) of relapsed patients had stressful life events in the pre-onset period, among which 80.5% had mania and 12% had depression. Family conflicts (33.7%), marital conflicts (12.4%) and the death of a close family member (6.7%) were the most commonly reported stressful life events. Stressful life events and poor social support have statistically significant association with relapse of bipolar disorder – 70.58% (60/85) of patients with strong social support had no stress or mild stress and the difference is statistically significant when compared with those patients with poor and moderate social support (Kocalevent and others, 2018).

Conclusion: Stressful life events and a greater severity of stress in the pre-onset period were risk factors for relapse, whereas strong social support helps in maintaining remission. Knowing the severity and impact of stressful life events and the strength of social support in the course of bipolar disorder helps in predicting further relapse and to modify the psychosocial factors, environmental factors, and social support systems.

Keywords

Bipolar Disorder, Relapse, Remission, Stressful Life Events, Social Support, South India

INTRODUCTION

Bipolar disorder (BD) is characterised by episodes in which mood and activity levels are significantly disturbed with some occasions of an elevation of mood and of others of lowering of mood (Akiskal and others, 2005). According to the World Health Organization, BD is the sixth leading cause of disability-adjusted life years in individuals aged 15-44 years (WHO, 2003). Irrespective of nationality, race, ethnic origin and socioeconomic status the prevalence of BD in the world's population is around 1% (Sagar & Pattanayak, 2017). Relapse in BD is the worsening or recurrence of manic, depressive, or mixed affective signs and symptoms after a period of eight weeks of a premorbid level of functioning. An increased frequency of relapse in BD can lead to high morbidity and mortality due to suicide, cognitive deficits and significant impairment in psychosocial functioning. Relapses have a huge impact on the economy, interpersonal relationships and quality of life of patients and their family members (Pompili and others, 2014). So, it is imperative to learn about the factors associated with relapse in BD.

'Life events' are defined as any significant changes in the personal surroundings of an individual that results in personal and social consequences (Aldinger & Schulze, 2017). Life events can be unexpected or be anticipated. Stressful life events are discrete quantifiable circumstances that can have a severe negative impact on the course of BD (Kumari & Jahan, 2006). There is well-established evidence on the role of genetic factors on the onset and course of BD. Epigenetics studies have found that genetic vulnerability for BD is potentiated by the early life events in an individual's life (Bergink and others, 2016). Most of the studies focused on the neurobiology of BD and not much significance was given to the environmental and psychosocial influences (Smoller & Finn, 2003). In spite of the influence of biological factors there are psychosocial factors influencing the onset, severity of episode, type, timing and outcome of the affective episode (El Kissi and others, 2013; Kemner and others, 2015). These psychosocial factors include personality traits, stressful life events, coping styles, perceived social support, social life of the person, early childhood adversities, and adherence to the prescribed medications.

There are several physiological mechanisms that explain the association between stressful life events and BD. Central nervous system involvement, catecholamines, glutamate, gamma amino butyric acid (GABA), immune cells, cytokines, endorphin-encephalins, hypothalamo-pituitary-adrenocortical and the adrenomedullary systems are involved in coping with stress, and modulate the stress response system in the body (Lau and others, 2013). Other theories related to stressful life events and BD are early adversity sensitisation, kindling/behavioural sensitisation, neurogenic hypothesis, and social rhythm disruption (Dienes and others, 2006). The full impact of stressful life events in the course of BD is poorly understood.

Social support may act as a buffer on effects of the stressful life events. Literature showed that the size of a social support system and the satisfaction with the support received from that support system are two different dimensions of social support (Kazan and others., 2019). If the individual is satisfied with the available social support systems which the person perceives then it can be an important and independent factor for coping with stress. Satisfying social support from family and friends and having good social relations have constructive consequences in preventing relapse in BD.

So, having strong social support will decrease social isolation and enhances the quality of life. Defects in the perceived social support can hamper a favourable outcome, reduce drug compliance, and can result in incomplete recovery. There are studies on social support and its association with the polarity of the episode, in others words, depressive episodes were predominant with low social support (Ellicott and others, 1990; Malkoff-Schwartz and others, 2000). Sometimes the illness itself can be a cause for disrupted social relations with care givers, family, and friends. Limited research has examined the impact of social support on the course of BD.

There is dearth of studies from India that assessed the impact of stressful life events and social support on BD. This study would help the clinician to know about the impact of stressful life events and social support on BD in a developing country like India.

As India is in the phase of urbanisation and industrialisation, there is increased psychological stress associated with modern busy life. Recognising the life events associated with the relapse of BD would advance the clinician's knowledge of the psychosocial stressors specific to the individual and helps in prolonged remission period with improved quality of life of patients. So, early identification of stress in patients with any psychiatric illness and providing adequate social support to cope with the stress could prevent future relapses. In patients with BD, poor social support can increase the vulnerability to stressful life events and can increase the severity of stress. It is important to know about the level of social support perceived by the patients who experienced stressful life events prior to the relapse. In spite of the influence of stress and poor social support there are other factors like sociodemographic and illness-related factors contributing to relapse.

The present study was planned to find the impact of stressful life events and social support among patients with BD. We also explored the association between relapse and sociodemographic and illness-related variables in the study.

MATERIALS AND METHODS

A cross-sectional descriptive study was carried out in the Department of Psychiatry, in a tertiary care centre in South India, over a period of one year from 1 March 2021. The study sample consisted

of 157 patients diagnosed with BD according to DSM-5 criteria (APA, 2013), either in relapse or in remission including both inpatients and outpatients who met the inclusion and exclusion criteria. In a study conducted by Sam and others, (2019) assessing stressful life events, the prevalence was found to be 69.5%. Using this data, assuming 90% confidence interval and 6% absolute precision, the minimum sample size required for the current study is calculated using the formula:

$$n = \frac{(Z_\alpha)^2 PQ}{d^2}$$

Zα= Z value of α error at 10% = 1.64

P= 69.5%

Q= 1-P

So, the calculated minimum sample size required is n= 157.

Operational definitions

These definitions were operationalised for this study after reviewing certain previous studies (Sam and others, 2019; Hirschfeld and others, 2007).

Relapse in BD: Worsening or reoccurrence of manic, depressive, or mixed affective signs and symptoms after a period of eight weeks of a premorbid level of functioning.

Remission in BD: No significant signs or symptoms of mood disturbance present over the past 2 months.

Pre-onset period: One month period back from the day of onset of symptoms, that is the day on which the informant started recognising that the patient is obviously abnormal and needs intervention.

Inclusion criteria

All diagnosed patients with BD according to DSM-5 criteria, either in relapse or in remission, in the age group of 18-65 years belonging to all genders, accompanied by a key informant, whose information was reliable and adequate. Written informed consent was obtained both from the patient and relative.

Exclusion criteria

Patients who were not willing to give consent, patients with intellectual disability, organic mood disorders, delirium, patients with substance dependence except nicotine, end-stage medical illness (such as chronic kidney disease, chronic liver disease, congestive heart failure) were excluded from the study.

Study tools

1. A semi-structured proforma for sociodemographic and illness-related data.

2. Young Mania Rating Scale [YMRS] is one of the most frequently utilised rating scale, clinician-administered to assess manic symptoms. The scale has 11 items, based on the patient's subjective report of their clinical condition over the previous 48 hours. There are four items in the YMRS which are graded on a 0 to 8 scale that includes irritability, speech, thought content and disruptive/aggressive behaviour, and the remaining seven items are graded on a 0 to 4 scale. These four items are given twice the weight of the others to compensate for poor cooperation from severely ill patients. The total score of all the items on the scale is summated between 0-60. A total score of ≤12 indicates remission, a score of 13-19 is minimal symptoms of mania, 20-25 is mild mania, 26-37 is moderate mania, and a score of 38-60 is severe mania (Young and others, 1978).

3. The Hamilton Depression Rating Scale [HAM-D] is the most widely used clinician-administered depression assessment scale. It contains a total of 17 items pertaining to symptoms of depression experienced over the past week. The total score is calculated by adding the individual scores from each question. The higher the total score the more severe the depression. A score of 0-7 is within the normal range and indicates remission. Score 7-17 represents mild depression, 18-24 represents moderate depression, and score 25 and above represents severe depression.

The maximum score is 52 on the 17-point scale (Hamilton and others, 1960).

4. Presumptive Stressful Life Events Scale [PSLES]. PSLES was developed by Singh and others, 1984. This scale consists of 51 life events relevant to Indian living conditions. Scale items classified as desirable, undesirable or ambiguous, and personal or impersonal. The desirable life events are pregnancy of a wife, marriage of daughter/dependent sister, major purchase or construction of house, appearing for examination or interview, getting married or

engaged, change of residence, change or expansion of business, outstanding personal achievement, gain of new family member and going on a pleasure trip or pilgrimage. The undesirable events include death of a spouse, extra marital relationship of spouse, suspension or dismissal from job, detention in jail of self or close family member, lack of child, death of close member, marital conflicts, property or crops damaged and death of friend. Each life event in the PSLES is given a mean stress score. Death of spouse is the stressful life event with highest mean stress score of 95, followed by extra marital relation of spouse with a stress score of 85. Going on a pleasure trip or pilgrimage is the life event with lowest stress score with a score of 20. The scale includes the life events in two categories, the life events in the past one year and life time events.

In the present study, we did not record the lifetime life events.

For patients in the relapse of BD, the life events in the pre-onset period were taken. In patients in remission, life events in the past one year and in the last episode of illness were taken. For patients with multiple stressful life events in the pre-onset period of relapse, the PSLES score is calculated by summating the mean stress score for each life event. For patients with multiple stressful life events in the pre-onset period, the stressful life event with the highest mean stress score is considered in precipitating the relapse. The severity was divided into three groups.

A score of <40 is no stress/mild stress, score of 41-200 is moderate stress, and a score of >200 severe stress (Singh and Kaur, 1984).

5. Oslo-3 Social Support Scale [OSSS-3] –consists of three items assessing the level of social support. The sum of the score ranges from 3 to 14 with higher values representing strong social support and lower values showing poor social support. The questions included in the scale comprised the number of people extending support in times of great personal problems, the amount of interest and concern others show in the patient, and how easy is it to get practical help from neighbours when in need. The first question on the scale was scored from 1-4 and the last two questions on the scale were given a score from 1-5. The total score is calculated by adding the individual scores from each question. The scores were operationalised into three levels of social support. A total score of 3-8 indicates poor social support, score of 9-11 shows moderate social support and a score of 12-14 indicates strong social support. (Kocalevent and others, 2018).

Method of data collection

The study protocol was approved by the Institutional Ethics Committee. After obtaining the institutional review board and ethical clearance, 157 patients with BD either in relapse or in remission, both inpatients and outpatients according to DSM-5 diagnostic criteria were included in the study by consecutive sampling after taking informed consent. A semi-structured proforma was used to collect sociodemographic details and illness-related factors by interview method both from the patient and the informant. Structured assessment was carried out using HAM-D and YMRS to assess the severity of the current episode and these scales are reapplied at the time of clinical remission (when the patient ceases to express mood symptoms) in patients with relapse. PSLES and OSSS-3 were applied once the patient was euthymic (YMRS:<12/HDRS:<7), OP patients were reviewed in the second or third week. The assessment of stressful life events and social support in patients with relapse was delayed, so that the affective symptoms or the psychotic symptoms would not affect the reporting of the stress and social support. All informants were close relatives or family members. Their role was to support the patient in their daily activities in the hospital and collaborate with our team in management. No patient without an informant was included in the study. All patients had relatives staying with them in the hospital. So no patient was excluded from the study for not having an informant. Stressful life events in the pre-onset period were assessed in patients with relapse and in patients in remission, the stressful life events during the last year were assessed. The objective assessment of the stressful life events in relapsed and remission patients were done with the PSLES scale. The severity of the perceived stress was assessed by summating the mean stress scores of all the individual life events experienced by the patient. For patients in relapse, the stressful life event with the highest mean stress score in the pre-onset period is considered as the precipitating factor of relapse.

Statistical analysis

The data was analysed and presented as frequency and percentages for categorical data and mean and standard deviation for continuous data.

Table 1. Sociodemographic details and illness-related data

Variables	Total sample(n=157)	Relapse N=89 (=100%) frequency (%)	Remission N=68 (=100%) frequency (%)	Chi square	p-value*
Age(years)				6.126	0.190
18-24	19	11(12.4)	8(11.8)		
25-34	40	21(23.6)	19(27.9)		
35-44	26	10(11.2)	16(23.5)		
45-54	38	24(27)	14(20.6)		
55-65	34	23(25.8)	11(16.2)		
Gender					
Male	75	45(50.6)	30(44.1)	0.642	0.261
Female	82	44(49.4)	38(55.9)		
Marital status					
Single	57	30(33.7)	27(39.7)	3.010	0.390
Married	83	48(53.9)	35(51.5)		
Separated/divorced	10	5(5.6)	5(7.4)		
Widowed	7	6(6.7)	1(1.5)		
Number of children					
None	73	36(40.4)	37(54.4)	9.863	0.020*
1-2	69	3(43.8)	30(44.1)		
3-4	13	12(13.5)	1(1.5)		
>4	2	2(2.2)	0(0)		
Religion					
Christian	74	36(40.4)	38(55.9)	6.140	0.189
Hindu	65	43(48.3)	22(32.4)		
Muslim	18	10(11.2)	8(11.8)		
Education					
Primary	50	29(32.6)	21(30.9)	5.923	0.205
Secondary	31	17(19.1)	14(20.6)		
Diploma	22	17(19.1)	5(7.4)		
Graduate	54	26(29.2)	27(41.2)		
Occupation					
Non professional	35	20(22.5)	15(22.1)	0.563	0.967
Professional	20	11(12.4)	9(13.2)		
Housewife	32	17(19.1)	15(22.1)		
Retired	8	4(4.5)	4(5.9)		
Unemployed	62	37(41.6)	25(36.8)		
Residence					
Rural	74	37(41.6)	37(54.4)	3.125	0.210
Urban	83	52(58.4)	31(45.6)		
Type of family					
Nuclear	130	73(82)	57(83.8)	2.232	0.693
Joint	18	11(12.4)	7(10.3)		
Extended	9	5(5.6)	4(5.9)		

Variables	Total sample(n=157)	Relapse N=89 (=100%) frequency (%)	Remission N=68 (=100%) frequency (%)	Chi square	p-value*
Family income (INR)					
₹1000-₹10000	9	4(4.5)	5(7.4)	22.005	<0.001*
₹11000-₹25000	75	57(64)	18(26.5)		
₹26000-₹50000	56	21(23.6)	35(51.5)		
>₹50000	17	7(7.9)	10(14.7)		
Medical comorbidities					
Yes	57	35(39.3)	22(32.4)	0.368	0.232
No	100	54(60.7)	46(67.6)		
Diabetes					
Yes	40	26(29.2)	14(20.6)	0.219	0.148
No	117	63(70.8)	54(79.4)		
Hypertension					
Yes	26	20(22.5)	6(8.8)	6.116	0.047*
No	131	69(77.5)	62(91.2)		
Hypothyroidism					
Yes	22	11(12.4)	11(16.2)	0.495	0.324
No	135	78(87.6)	57(83.8)		
Family h/o psychiatric illness					
Yes	99	57(64)	42(61.8)	0.769	0 .449
No	58	32(36)	26(38.2)		
Family h/o bipolar disorder					
Yes	74	41(46.1)	33(48.5)	0.759	0.442
No	83	48(53.9)	35(51.5)		
Total duration of illness					
0-5 years	25	14(15.7)	11(16.2)	0.442	0.802
5-10 years	40	21(23.6)	19(27.9)		
>10 years	92	54(60.7)	38(55.9)		
Age at onset of illness					
<18years	47	27(30.3)	20(29.4)	3.290	0.510
18-24 years	59	29(32.6)	30(44.1)		
25-34 years	35	22(24.7)	13(19.1)		
35-44 years	15	10(11.2)	5(7.4)		
>44 years	1	1(1.1)	0(0)		
Number of previous episodes					
1-5	90	49(55.1)	41(60.3)	0.552	0.759
6-10	33	19(21.3)	14(20.6)		
>10	34	21(23.6)	13(19.1)		

Variables	Total sample(n=157)	Relapse N=89 (=100%) frequency (%)	Remission N=68 (=100%) frequency (%)	Chi square	p-value*
Total number of manic episodes					
0	5	5(5.6)	0(0)	5.339	0.254
1-5	106	57(64)	49(72.4)		
6-10	28	16(18)	12(17.60)		
11-15	13	7(7.90)	6(8.80)		
16-20	5	4(4.50)	1(1.50)		
>20	0	0.00%	0.00%		
Number of depressive episodes					
0	47	26(29.2)	21(30.9)	0.802	0.670
1-5	109	62(69.7)	47(69.1)		
6-10	1	1(1.1)	0(0)		
Number of mixed episodes					
0	137	78(87.6)	59(86.8)	1.859	0.395
1-5	18	9(10.1)	9(13.2)		
6-10	2	2(2.2)	0(0)		
Index episode polarity					
Mania	88	46(51.7)	42(61.8)	4.848	0.089
Depression	67	43(48.3)	24(35.3)		
Mixed	2	0(0)	2(2.9)		
Polarity of current episode					
Mania		73(82)			
Depression		15(16.90)			
Mixed		1(1.10)			
Stressful life event in pre-onset period of relapse					
Yes		67(75.3)			
No		22(24.7)			

(*p value <0.05 is statistically significant).

For further analysis continuous variables such as age were classified into appropriate groups. Association between relapse and stressful life events, social support, sociodemographic and illness-related variables were tested for statistical significance using Chi-square/Fisher's exact tests. A p-value of less than 0.05 was considered as statistically significant.

RESULTS

Demographic and illness-related characteristics of the subjects

Among the 157 BD patients, 56.7% (89/157) had a relapse episode and 43.3% (68/157) were in remission. Sociodemographic details and illness-related details of both the relapse and remission groups and the association of the variables with the relapse were given in Table 1. The mean age of the study population was 41.08± 13.34 years. The mean age of patients with relapse was 42.48±13.60 years and in remission was 39.23±12.86 years. 47 of 89 patients were above the age of 44 in the relapse group and in the remission group, a greater number of patients were in the age group of 25 to 34 years and the difference is not statistically significant. Among patients with relapse, 50.6% (45/89) were males and 49.4% (44/89) were females and in patients in remission 44.1% (30/68) were males and 55.9% (38/68) were females. Of all the relapsed BD 83%

(73/89) had mania.

Table 1 shows the association of relapse with sociodemographic and illness-related data.

Stressful life events and relapse

Among relapsed patients 75.3% (67/89) had stressful life events in the pre-onset period. 73.3% (33/45) of male patients with relapse of BD reported stressful life events in pre-onset period and females reported 77.3% (34/44). In relapsed patients the most frequently reported stressful life event was family conflict (33.7%), followed by marital conflicts (12.4%) and the death of a close family member (6.7%).

Type and distribution of pre-onset stressful life events are given in Table 2. Among relapsed males the stressful life events commonly reported are family conflicts, marital conflicts, broken engagement/love affair, detention in jail of self/close family member. In relapsed females, the commonly reported stressful life events are family conflicts, conflicts with in-laws, marital conflicts, death of a close family member, and major illness or injury. Among patients in remission, the reported stressful life events are family conflicts (30.9%), conflicts with in-laws (other than dowry (10.3%), trouble at work with colleagues (5.9%). Male patients in remission reported family conflict as the common stressful life event and females in remission reported family conflict followed by conflicts with in-laws (other than dowry) as the stressful life event.

The mean duration between the stressful life events and relapse was 7.61± 6.15 days.

Table 3 shows the association of severity of stressful life events and relapse in BD (df-degrees of freedom) (*p value <0.05 is statistically significant).

Table 2. Type and distribution of pre-onset stressful life events

Type of pre-onset stressful life events	n(%)
Family conflict	30(33.7)
Marital conflict	11(12.6)
Death of close family member	6(6.7)
Marital separation/divorce	4(4.5)
Major personal illness or injury	4(4.5)
Broken engagement/love affair	4(4.5)
Detention in jail of self/close family member	4(4.5)
Death of spouse	3(3.4)
Conflicts with in-laws (other than dowry)	3(3.4)
Illness of family member	3(3.4)
Change in working conditions or transfer	2(2.2)
Self or family members unemployed	2(2.2)
Change of residence	2(2.2)
Death of friend	2(2.2)
Appearing for an interview or examination	2(2.2)
Conflicts with in-laws (other than dowry)	1(1.1)
Son or daughter leaving home	1(1.1)
Suspension or dismissal from job	1(1.1)
Trouble at work with colleagues	1(1.1)
Beginning or ending school	1(1.1)
Minor violation of law	1(1.1)
Getting married/engaged	1(1.1)
Total	89(100)

Table 3. Severity of stressful life events in both relapse and remission group

Severity of stressful life events	Total sample(n=157)	Relapse (n=89) (%)	Remission (n=68)(%)	Chi square (df)	p-value*
Mild stress/no stress	100	52(58.4)	48(70.6)	10.087 (2)	0.006*
Moderate stress	45	25(28.1)	20(29.4)		
Severe stress	12	12(13.5)	0(0)		

Among patients in remission, about 70.6% had mild or no stress and the difference is statistically significant when compared with patients in relapse (chi square =10.087, df=2, p-value= 0.006). Among patients who had severe stress, all of them had relapses and no patient in remission experienced severe stress. So the severity of stressful life events is associated with a relapse.

Table 4 indicates that among patients with relapse, 51.7% (46/89) had stressful life events in the last episode of illness and in patients in remission, 75% (51/68) had stressful life events as a precipitating factor in the previous episode. It is found to be statistically significant (chi square=8.874, df=1, p-value 0.002) and is associated with relapse (df-degrees of freedom) (*p value <0.05 is statistically significant).

About 70.58% (60/85) of patients with strong social support had no stress or mild stress and a statistically significant association was found between severity of stressful life events and level of social support in BD (chi square=11.406, df=4, p=0.026) (Table 5). (df-degrees of freedom) (*p value <0.05 is statistically significant).

Table 4. Association between relapse and stressful life events in last episode.
Statistically significant association found between relapse and stressful life events in last episode, (p value<0.05 indicates statistical significance)

Stressful life events in the last episode	Relapse n=89(100%)	Remission N=68(100%)	Chi square (df)	p-value*
Present	46(47.4%)	51(52.6%)	8.874 (1)	0.003*
Absent	43(71.7%)	17(28.3%)		
Total	89	68		

Table 5. Association of level of social support and severity of stressful life events in pre-onset period

Level of social support	Mild/no stress	Moderate stress	Severe stress	Chi-square (df)	p-value*
Poor social support	25(60.97)	15(36.58)	1(2.43)	11.406 (4)	0.0264*
Moderate social support	15(48.38)	14(45.16)	2(6.45)		
Strong social support	60(70.58)	16(18.82)	9(10.58)		

Table 6. Association of perceived social support and stressful life events in the pre-onset period of relapse

Level of social support	Stressful life events in pre-onset period of relapse		Chi square (df)	p-value*
	Yes	No		
Poor social support	31 (46.26)	21 (95.45)	20.993 (2)	<0.001*
Moderate social support	24 (35.82)	1 (4.54)		
Strong social support	12 (17.91)	0 (0.00)		
Total	67 (100.0%)	22(100.0%)		

In table 6 about 46.26% (31/67) of patients with stressful life events in the pre-onset period had poor social support which is statistically significant. (Chi square= 20.993, df=2, p=<0.001). (df-degrees of freedom) (*p value <0.05 is statistically significant).

Social support and remission

Table 7. Level of social support in both relapse and remission group

Level of social support	Total sample (n=157)	Relapse (n=89)	Remission (n=68)	Chi square (df)	p-value*
Poor social support	41	35(39.3)	6(8.80)	35.005 (2)	<0.001*
Moderate social support	31	24(27.0)	7(10.30)		
Strong social support	85	30(33.70	55(80.90)		

Association between level of social support and relapse in BD. (df-degrees of freedom) (*p value <0.05 is statistically significant).

80.9% (55/68) of patients in remission have strong social support, and in relapsed patients, it is 33.7% (30/89), and the difference is statistically significant (chi square=35.005, df=2, p<0.001). So, strong social support had statistically significant association with reduced relapse, respectively remission of BD.

Table 8. Association between social support and socio-demographic variables in patients with bipolar disorder

Socio-demographic variable		Level of Social Support			Chi square	p-value*
		Mild	Moderate	Strong		
Age interval (in years)	18-24	8(19.51%)	1(3.22%)	10(11.76%)	14.103	0.079
	25-34	7(17.07%)	7(22.58%)	26(30.58%)		
	35-44	7(17.07%)	3(9.67%)	16(18.82%)		
	45-54	7(17.07%)	13(41.93%)	18(21.17%)		
	55-65	12(29.26%)	7(22.58%)	15(17.64%)		
Gender	Male	20(48.78%)	16(51.61%)	39(45.88%)	0.322	0.851
	Female	21(51.21%)	15(48.38%)	46(54.11%)		
Marital status	Single	13(31.70%)	10(32.25%)	34(40%)	5.626	0.466
	Married	20(48.78%)	18(58.06%)	45(52.94%)		
	Separated/Divorced	4(9.75%)	2(6.45%)	4(4.70%)		
	Widowed	4(9.75%)	1(3.22%)	2(2.35%)		
Number of children	None	16(39.02%)	12(38.70%)	45(52.94%)	6.963	0.336
	1-2	19(46.34%)	15(48.38%)	35(41.17%)		
	3-4	6(14.63%)	3(9.67%)	4(4.70%)		
	>4	0(0.0%)	1(3.22%)	1(1.17%)		
Religion	Christian	14(34.14%)	15(48.38%)	45(52.94%)	10.089	0.259
	Hindu	24(58.53%)	14(45.16%)	27(31.76%)		
	Muslim	3(7.31%)	2(6.45%)	13(15.29%)		
Education	Primary	16(39.02%)	13(41.93%)	21(24.70%)	29.404	<0.001*
	Secondary	6(14.63%)	4(12.90%)	21(24.70%)		
	Diploma	11(26.82%)	8(25.80%)	3(3.52%)		
	Graduate	8(19.51%)	6(19.35%)	40(47.05%)		

Socio-demographic variable		Level of Social Support			Chi square	p-value*
		Mild	Moderate	Strong		
Occupation	Non-professional	9(21.95%)	10(32.25%)	16(18.82%)	6.414	0.600
	Professional	5(12.19%)	2(6.45%)	13(15.29%)		
	Housewife	7(17.07%)	9(29.03%)	16(18.82%)		
	Retired	3(7.31%)	1(3.22%)	4(4.70%)		
	Unemployed	17(41.46%)	9(29.03%)	36(42.35%)		
Type offamily	Nuclear	31(75.60%)	25(80.64%)	74(87.05%)	16.205	0.040*
	Joint	5(12.19%)	6(19.35%)	9(10.58%)		
	Extended	5(12.19%)	0(0.0%)	2(2.35%)		
Type of Residence	Rural	17(41.46%)	14(45.16%)	43(50.58%)	1.980	0.739
Total family income (INR)	1000-10000	4(9.75%)	0(0.0%)	5(5.88%)	14.336	0.026*
	10001-25000	26(63.41%)	18(58.06%)	31(36.47%)		
	25001-50000	8(19.51%)	11(35.48%)	37(43.52%)		
	>50000	3(7.31%)	2(6.45%)	12(14.11%)		

Table 9. Association between social support and illness-related variables in patients with bipolar disorder

Illness related variables		Social support			Chi square	p-value*
		Poor	Moderate	Strong		
Family h/o psychiatric illness	Present	26(63.41%)	16(51.61%)	57(67.05%)	2.329	0.312
	Absent	15(36.58%)	15(48.38%)	28(32.94%)		
Medical comorbidities	Present	11(26.82%)	18(58.06%)	28(32.94%)	8.355	0.015*
	Absent	30(73.17%)	13(41.93%)	57(67.05%)		
Total duration of illness	0-5 Years	8(19.51%)	1(3.22%)	16(18.82%)	5.545	0.236
	5-10 Years	11(26.82%)	7(22.58%)	21(24.70%)		
	>10 Years	22(53.65%)	23(74.19%)	48(56.47%)		
Age at onset of illness	<18 Years	13(31.70%)	8(25.80%)	26(30.58%)	12.535	0.129
	18-24 Years	10(24.39%)	12(38.70%)	37(43.52%)		
	25-34 Years	14(34.14%)	5(16.12%)	16(18.82%)		
	35-44 Years	4(9.75%)	5(16.12%)	6(7.05%)		
	>44 Years	0(0.0%)	1(3.22%)	0(0.0%)		
Number of previous episodes	1-5	21(51.21%)	17(54.83%)	52(61.17%)	2.450	0.654
	5-10	11(26.82%)	8(25.80%)	14(16.47%)		
	>10	9(21.95%)	6(19.35%)	19(22.35%)		

Statistically significant association was found between social support and variables like education, type of family and total family income. About 47.05% of patients with strong social support were graduates and the difference when compared with other educational status is statistically significant. (Chi square= 29.404, df=6, p value=<0.001). About 87.05% (74/85) of patients who receive strong social support belong to the nuclear family and the difference when compared with joint and extended family is statistically significant. (chi square=16.205, df=4, p value=0.04). About 53% (49/85) of patients

who received strong social support belong to an upper-middle-class family and the difference when compared with other socioeconomic class is statistically significant. (chi square=14.336, df=6, p value=0.026).

About 67.05% (57/85) of patients with BD who received strong social support did not have any medical comorbidity and the difference was found statistically significant (Chi square=8.355, df=2, p=0.015).

DISCUSSION

Sociodemographic and clinical profile

Among 157 BD patients, 89 patients relapsed and 68 patients remained in remission during the one-year observation period. In the present study the age of patients with BD ranged from 18 years to 65 years with mean age of the study population is 41.08 ± 13.34 years. Mean age of patients with relapse is 42.48 ±13.60 years and in patients with remission is 39.23±12.86 years. This finding is similar to that of the studies done by Subramanian and others, 2017; Chatterjee and others, 1989 and Kemner and others, 2015. The majority of the patients belong to the younger age group between 25 to 34 years, followed by patients in the age group of 45 to 54 years of age. Among relapsed patients, the majority were above 45 years of age, and in the remission group, the majority were below 45 years of age. The study showed that patients in the younger age group remained in remission. This is similar to the findings from other studies (Arnold and others, 2021; Coryell and others, 2009). But no statistically significant association found between age distribution and relapse. This was consistent with the reports from the study of Selvakumar and others, 2018, where no significant association was found between age distribution and relapse. Female patients remain in remission more often when compared to males, and relapses are more commonly seen in males than females, but the difference is not statistically significant. This can be explained as most of the females in the remission group were married and they have better social support systems when compared to males, which is similar to previous studies (Kawa and others, 2005; Shaik and others, 2017. The study by Davarinejad and others, 2021, found that the frequency of relapse was higher in men than in women and gender had no significant effect on relapse which is similar to the present study. This finding is contrary to the findings of the study done by Merikangas and others, 2007. All individuals in the present study had a minimum of primary education. The overall educational status of the study population was high when compared to other parts of India. This could be due to higher literacy rates of Kerala state in India. Among relapsed patients greater number of patients had primary education and in remission the majority were graduates, but the difference is not statistically significant. Sociodemographic correlates from another study by Merikangas and others, 2007 showed that BD is inversely related to educational level. Unemployment is a major problem in both relapse and remission group. This is significant as engaging in a satisfying occupation can reduce stress and provide better social support. In a study done by Miasso and others, 2012, in Brazil showed that only 14.8% of the interviewed people had a formal job which is much lower than the present study. Another study done by Jones and others, 2005, in Norway found that, when patients with BD are in remission, they are capable of keeping up a good performance at work. In the present study, among the relapsed patients the majority were married and this is contrary to the findings of the study done by Merikangas and others, 2007, were relapse occurred more frequently in divorced individuals. A greater number of patients in relapse belong to an urban residence when compared to patients in remission and the difference is not statistically significant. As India is a developing country with progressing urbanisation the recent migration of a large rural population to urban regions can be a risk factor for relapse in BD. The majority of patients in relapse were from a nuclear family when compared with patients in remission and the difference is not statistically significant. This is similar to the findings from the study done by Sam and others, 2019. The majority of the study sample have a family income between INR 10,000 to 25,000 per month. 64% of patients in relapse had a total monthly income of INR <25,000 and in patients with remission 51.5% had a total monthly income of INR >26,000, with the difference being statistically significant. This can be explained as better living condition and an upper socio-economic status can reduce the perceived stress and so decreases the frequency of relapse in BD. The patients who have frequent relapses are subject to more financial problems as they have to afford the cost of hospitalisation and expenses during an episode of illness. In the present study the age of onset of illness in the majority of the study sample was between 18-24 years. Only 1% had an age of

onset above 44 years. This is consistent with findings from another studies by Chopra and others, 2006; Judd and others, 2002; Backlund and others, 2009. A greater number of patients in the relapse group had an age of onset of illness between 18-24 years, but the difference is not statistically significant. The majority of the patients were found to have a total duration of more than 10 years which is consistent with the chronicity of BD and is similar to the study by Negash and others, 2005. This study found that the BD run a severe clinical course in developing country settings than in developed countries. Most of the patients in the study sample had 1-5 episodes of either mania or depression in their lifetime which is similar to the findings of study by Solomon and others, 2010. The majority of patients had the index episode as mania which is similar to other studies. (Subramanian and others, 2017; Chopra and others, 2006; Khanna and others, 1992; Backlund and others, 2009). This is in contrast to studies from Europe, where index depression is more frequent (Daban and others, 2006; Judd and others, 2002; Perugi and others, 2000).

Stressful life events and relapse

Among the relapsed patients about 75.3% (67/89) had stressful life events with in 1 month prior to the relapse. There is an association with stressful life events and the relapse of BD which is similar to the findings in the study done by Yadav and others, 2016. Another study from South India showed more than one-third of total episodes were precipitated by stressful life events (Subramanian and others, 2017).

So stress has a negative impact in the course of BD resulting in the decreased threshold for stress and sensitising the individual to stressful life events. This is similar to the high prevalence of stressful life events during the pre-onset period of relapse reported in other studies from India (Nisha and others, 2015; Chatterjee & Kulhara, 1989). Another study from South India showed that episode frequency was significantly associated with high expressed emotions, poor treatment adherence and high stressful life events (Issudeen & Saji, 2018). There are studies that reported findings similar to that of the present study, which proposed a negative impact of stressful life events on the course of BD (Joffe and others, 1989; Kennedy and others, 1983; Christensen and others, 2003; Ellicott and others, 1990; Swendsen and others, 1995. Studies by Johnson and others, 2003; McPherson and others, 1993; Pardoen and others, 1996, do not reveal an association between stressful life events and relapses and are contrary to the results of the present study. In the present study manic relapses are more in number than the depressive and mixed episodes of relapse. Among the relapsed patients with pre-onset stressful life events, mania (81%) was found to outnumber depression (12%) which is contrary to the results of studies from Western literature that reported depression as a predominant course of BD (Judd and others, 2002). Results similar to our study which reported a greater number of manic relapses is seen in other studies on BD from tropical regions like India, Nigeria and Hong Kong (Mathew and others, 2022; Subramanian and others, 2017). This is hypothesised to be due to the influence of bright sunlight and a less variable day-night cycle on the zeitgeber (Narayanaswamy and others, 2014).

This can also be due to the recall bias, that the proclivity of patients and family members in recollecting the disruptive manic episodes and failure of recall about the depressive episodes leading to less reporting of the depressive episodes.

Among relapsed males the stressful life events commonly reported are family conflicts, marital conflicts, broken engagement/love affair, detention in jail of self/close family member. In relapsed females the commonly reported stressful life events are family conflicts, conflicts with in-laws, marital conflicts, death of a close family member, and major illness or injury. Male patients in remission reported family conflict as the common stressful life event and females in remission reported family conflict followed by conflicts with

in-laws (other than dowry) as the stressful life events. The patients in remission experience less stress compared to the relapsed patients. There may be other factors like strong social support which help the remission group to remain symptom free. In our study, in patients with both relapse and remission, the stressors were predominantly from the family and social contexts which is contrary to the reports from other studies. Bereavement was found to be the major life event in a study by Ambelas and others, 1979. Personal physical illness and illness in the family were the common stressful life events reported by Hunt and others, 1992, death of first degree relative, economic crisis, failure in any achievement, and the death of a spouse were the most frequent stressors reported by Singh and others, 1984. These

differences in reported stressful life events can be due to cultural factors, geographical differences, seasonal factors, different methodologies of study, the use of different rating scales for quantifying stressful life events, and the different

pre-onset period defined in other studies (Miklowitz and others, 1988). Marital and family conflicts, health problems, emotional and ambition failures, lack of success, and work overload were the reported stressful life events in a study by Bidzińska and others, 1984, which is similar to the reported stressful life events in our study group.

In the present study, the mean time period between pre-onset stressful life events and relapse was 7.61± 6.15 days. This is different from other studies in India (Sam and others, 2019) where the mean time period between stressful life events and relapse was 19.73±4.9 days. The effect of those stressful life events which occurred shortly before relapse indicates that such life events have an acute, rather than a delayed effect on the risk of relapse and it showed that stressful life events are the major cause of the relapse rather than other factors like comorbid personality disorders, substance use, expressed emotion, or medication adherence. In spite of the differences in the social and cultural factors this finding of our study is similar to the findings from the research done by Simhandl and others, 2015 and Gershon and others, 2013. Among the relapsed and remission patients a greater number of patients had stressful life events as the precipitating factor in the last episode of illness and the difference is statistically significant. Though the patients in remission had stressful life events in the previous episode, the strong social support perceived by them help them to remain in remission. Patients in remission received strong support from family, friends, caregivers, and from neighbours that help them to cope with the stressors in life and remain symptom-free. In relapsed patients they were sensitised by the stressful life events in the previous episode and the greater severity of stressful life event in the pre-onset period led to the current episode of illness. As the number of significant stressors increases over the lifespan of an individual then the chances of relapse are high and the episodes can be precipitated even with mild stress. This finding is similar to the stress sensitisation hypothesis by Post and others, 1992, which states that stressful life events precipitate initial episodes of BD, while the subsequent episodes become autonomous from external influence (Post and others, 2001). Thus, due to this sensitisation to stress, even mild stress itself can precipitate an episode. So, the impact of stressful life events in the course of BD is of relevance to the treating psychiatrist to identify the life events specific to each patient and to intervene early. This can influence the outcome of the illness as the episodes precipitated by stressful life events had a better prognosis. Another study by Ellicott and others, 1990 and Malkoff-Schwartz and others, 2000, found that higher levels of stress were direct predictors of relapse which is similar to the present study. In the present study, patients with stressful life events in the pre-onset period had poor social support which added to their stress vulnerability and led to relapse. This is similar to the findings from the study done by Johnson and others, 2003. If the patients had strong social support, they could have managed the stressors of life and would have prevented another episode of illness. So social support is another important factor in the course of BD.

Social support and remission

Our study showed that majority of patients in remission had strong social support when compared with patients in relapse and the difference is statistically significant. This is similar to previous studies that showed that social support can have an impact on the course of BD (Wilkins and others, 2004). Social support had a significant role in the

socio-occupational functioning of patients during the remission period. In relapsed patients a greater number of patients had poor social support and this would have contributed to perceiving greater stress in the pre-onset period. In our study we found that among patients who had stressful life events in the pre-onset period, the majority of them had poor social support. So, poor social support can have a negative impact in the course of BD. In the present study females received strong social support when compared to males but the difference is not statistically significant. This is because the majority of the female sample included in the study were married and received better social support from family. Among patients with strong social support the majority were married, but the difference is not statistically significant and this is similar to the findings from the study done by Johnson and others, 2003. Among patients who had strong social support greater number of patients were graduates. Statistically significant association was found between education and social support among bipolar patients. The type

of family and total monthly income of the family was found to be associated with social support. Strong social support was received by patients belonging to the nuclear family. In the modern era, there is a greater prevalence of nuclear families, and though it caused increased stress to patients, it also facilitated better care and support. Most of the patients who received strong social support belong to an upper-middle-class family, which shows that having a good education and a better standard of living can influence the perceived social support and can be protective factors in the course of BD.

In our study, strong social support was received by patients without any medical co-morbidities. This shows that caregiver burden is another factor in which the caregivers find it difficult to manage patients with medical problems as well.

The present study showed that relapsed patients received less social support when compared to patients in remission. It is similar to the results of the study conducted in Sweden by Johnson and others, 2003. He found the relationship between inadequate social support and incomplete recovery in a one-year follow-up study of 94 patients with BD. In a study by Cohen and others (2004), higher levels of stress and lower levels of social support predicted depressive recurrence. In the present study we found that the greater severity of stress and the poor social support in the pre-onset period led to relapse. We also found that, in patients in remission strong social support helps them to remain symptom free and prolong the remission. Literature had similar studies which reported the influence of social support in remission (Kulhara and others, 1999; O'Connell and others, 1985; Weinstock and Miller, 2010; Johnson and others, 1999. These studies also showed that poor social support can be risk factor for relapse and they predicted depressive relapse. In another study done by Staner and others, 1997, found that social support does not predict relapse and is not a major factor in the recovery of the individual. This is contrary to the findings of the present study. The poor social support can also be ascribed as the illness itself disrupting social relations like during a manic episode, the aggression and irritability of the patient towards caregiver, family, friends and neighbours lead to reduced social interaction with the patient resulting in social isolation. The poor social support can also be due to the caregiver burden, especially in patients with longer duration of illness and frequent relapses. Our study did not explore the caregiver burden of family members of the patient.

Better social support helps the patients to have good drug compliance, better coping skills, and improved quality of life.

Social support had a significant role in the socio-occupational functioning of patients during the remission period. The social support perceived by an individual nourishes mental health and prevents future relapses (Kallivayalil and Enara, 2022). Preventive psychiatry is important in helping the patient to prolong the period of remission and prevent relapses (Kallivayalil and Chadda, 2017).

STRENGTHS AND LIMITATIONS

The strengths of our study were that we assessed both remission and relapse patients so that the clinical variables were compared. Also, we assessed the patients with relapse after they attain clinical remission so that the affective symptoms or psychotic symptoms do not influence the reporting of stressful life events and perceived social support. We have assessed both social support and stress among patients with BD which was not been studied previously in South India. There were some limitations to our study. The sample is constituted by inpatients and outpatients in a tertiary care hospital which does not represent patients with BD in the general population. Factors like medication adherence, expressed emotions, caregiver burden, and personality traits can be independent predictors of relapse and were not assessed in our study. Life events included in the PSLES were only included and remote stressful life events causing early adversity sensitisation were not assessed. Psychotic symptoms and the severity associated with them were not assessed in our study. Social support was assessed confining to the rating scale alone and other aspects of social life were not assessed in detail. We studied only a limited number of variables associated with stressful life events and social support. Follow-up studies would help in better understanding the impact of stressful life events and social support in the course of BD.

CONCLUSION

This study emphasised the impact of stressful life events and social support on the course of BD. Understanding the role of stressful life events and social support would help in predicting further relapse and modifying the psychosocial factors,

environmental factors, and social support systems. Family conflicts, marital conflicts, and death of a close family member were the commonly reported stressful life events in our study.

So psychotherapeutic interventions like family therapy, marital therapy, and cognitive behavioural interventions focusing on resolving the stress in family and social life will improve the quality of life. By educating the caregivers about the impact of social support on the course of BD and encouraging them to give better social support to patients. So important avenues for future research can include factors like personality profile, coping styles, medication adherence, different dimensions of social support and social life, and plans for a community-based study with a larger sample and follow-up study on those patients. This helps the clinician to develop advanced pharmacological and non-pharmacological methods to prolong remission and improve the quality of life of patients with BD.

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REFERENCES

Akiskal HS. Mood disorders: historical introduction and conceptual overview. B Sadock, V Sadock (Eds.), Comprehensive Textbooks of Psychiatry. 2005.

Aldinger F, Schulze TG. Environmental factors, life events, and trauma in the course of bipolar disorder. Psychiatry Clin Neurosci. 2017 Jan;71(1):6-17. doi: 10.1111/pcn.12433. Epub 2016 Sep 21. PMID: 27500795; PMCID: PMC7167807.

Ambelas A. Psychologically stressful events in the precipitation of manic episodes. Br J Psychiatry. 1979 Jul;135:15-21. doi: 10.1192/bjp.135.1.15. PMID: 497617.

Arnold I, Dehning J, Grunze A, Hausmann A. Old age bipolar disorder-epidemiology, aetiology and treatment. Medicina (Kaunas). 2021 Jun 8;57(6):587. doi: 10.3390/medicina57060587. PMID: 34201098; PMCID: PMC8226928.

Backlund L, Ehnvall A, Hetta J, Isacsson G, Agren H. Identifying predictors for good lithium response - a retrospective analysis of 100 patients with bipolar disorder using a life-charting method. Eur Psychiatry. 2009 Apr;24(3):171-7. doi: 10.1016/j.eurpsy.2008.12.009. Epub 2009 Mar 14. PMID: 19286354.

Bergink V, Larsen JT, Hillegers MH, Dahl SK, Stevens H, Mortensen PB, et al., Childhood adverse life events and parental psychopathology as risk factors for bipolar disorder. Transl Psychiatry. 2016 Oct 25;6(10):e929. doi: 10.1038/tp.2016.201. PMID: 27779625; PMCID: PMC5290348.

Bidzińska EJ. Stress factors in affective diseases. Br J Psychiatry. 1984 Feb;144:161-6. doi: 10.1192/bjp.144.2.161. PMID: 6704602.

Chatterjee S, Kulhara P. Symptomatology, symptom resolution and short term course in mania. Indian J Psychiatry. 1989 Jul;31(3):213-8. PMID: 21927386; PMCID: PMC2992115.

Chopra MP, Kishore Kumar KV, Subbakrishna DK, Jain S, Murthy RS. The course of bipolar disorder in rural India. Indian J Psychiatry. 2006 Oct;48(4):254-7. doi: 10.4103/0019-5545.31559. PMID: 20703347; PMCID: PMC2915598.

Christensen EM, Gjerris A, Larsen JK, Bendtsen BB, Larsen BH, Rolff H, Ring G, Schaumburg E. Life events and onset of a new phase in bipolar affective disorder. Bipolar Disord. 2003 Oct;5(5):356-61. doi: 10.1034/j.1399-5618.2003.00049.x. PMID: 14525556.

Cohen AN, Hammen C, Henry RM, Daley SE. Effects of stress and social support on recurrence in bipolar disorder. J Affect Disord. 2004 Oct 1;82(1):143-7. doi: 10.1016/j.jad.2003.10.008. PMID: 15465589.

Coryell W, Fiedorowicz J, Solomon D, Endicott J. Age transitions in the course of bipolar I disorder. Psychol Med. 2009 Aug;39(8):1247-52. doi: 10.1017/S0033291709005534. Epub 2009 Apr 1. PMID: 19335937; PMCID: PMC3551474.

Daban C, Colom F, Sanchez-Moreno J, García-Amador M, Vieta E. Clinical correlates of first-episode polarity in bipolar disorder. Compr Psychiatry. 2006 Nov-Dec;47(6):433-7. doi: 10.1016/j.comppsych.2006.03.009. Epub 2006 May 26. PMID: 17067865.

Davarinejad O, Majd TM, Golmohammadi F, Mohamadi P, Radmehr F, Nazari S, Moradinazar M. Factors influencing the number of relapse in patients with bipolar I disorder. Shiraz E-Medical Journal. 2021 Aug 31;22(8).

Diagnostic and Statistical Manual of Mental Disorders : DSM-5. 5th ed. Washington, D.C: American Psychiatric Association, 2013;NLM unique ID 101604226.

Dienes KA, Hammen C, Henry RM, Cohen AN, Daley SE. The stress sensitization hypothesis: understanding the course of bipolar disorder.

J Affect Disord. 2006 Oct;95(1-3):43-9. doi: 10.1016/j.jad.2006.04.009. Epub 2006 Jul 11. PMID: 16837055.

El Kissi Y, Krir MW, Ben Nasr S, Hamadou R, El Hedda R, Bannour S, Ben Hadj Ali B. Life events in bipolar patients: a comparative study with siblings and healthy controls. J Affect Disord. 2013 Oct;151(1):378-83. doi: 10.1016/j.jad.2013.05.098. Epub 2013 Jul 4. PMID: 23830000.

Ellicott A, Hammen C, Gitlin M, Brown G, Jamison K. Life events and the course of bipolar disorder. Am J Psychiatry. 1990 Sep;147(9):1194-8. doi: 10.1176/ajp.147.9.1194. PMID: 1974746.

Gershon A, Johnson SL, Miller I. Chronic stressors and trauma: prospective influences on the course of bipolar disorder. Psychol Med. 2013 Dec;43(12):2583-92. doi: 10.1017/S0033291713000147. Epub 2013 Feb 18. PMID: 23419615; PMCID: PMC3748240.

Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960 Feb;23(1):56-62. doi: 10.1136/jnnp.23.1.56. PMID: 14399272; PMCID: PMC495331.

Hirschfeld RM, Calabrese JR, Frye MA, Lavori PW, Sachs G, Thase ME, Wagner KD. Defining the clinical course of bipolar disorder: response, remission, relapse, recurrence, and roughening. Psychopharmacol Bull. 2007;40(3):7-14. PMID: 18007564.

Hunt N, Bruce-Jones W, Silverstone T. Life events and relapse in bipolar affective disorder. J Affect Disord. 1992 May;25(1):13-20. doi: 10.1016/0165-0327(92)90088-n. PMID: 1624643.

Issudeen M, Saji PG. A comparative study on the psychosocial and treatment factors in frequency of episodes in bipolar affective disorder. Journal of Evolution of Medical and Dental Sciences. 2018 Feb 26;7(9):1075-82. doi: 10.14260/jemds/2018/245.

Joffe RT, MacDonald C, Kutcher SP. Life events and mania: a case-controlled study. Psychiatry Res. 1989 Nov;30(2):213-6. doi: 10.1016/0165-1781(89)90162-5. PMID: 2616687.

Johnson L, Lundström O, Aberg-Wistedt A, Mathé AA. Social support in bipolar disorder: its relevance to remission and relapse. Bipolar Disord. 2003 Apr;5(2):129-37. doi: 10.1034/j.1399-5618.2003.00021.x. PMID: 12680903.

Jones MM. The experience of bipolar disorder at work. International Journal of Psychosocial Rehabilitation. 2005 Jul 1;10(1).

Judd LL, Akiskal HS, Schettler PJ, Endicott J, Maser J, Solomon DA, Leon AC, Rice JA, Keller MB. The long-term natural history of the weekly symptomatic status of bipolar I disorder. Arch Gen Psychiatry. 2002 Jun;59(6):530-7. doi: 10.1001/archpsyc.59.6.530. PMID: 12044195.

Kallivayalil RA, Chadda RK. Preventive psychiatry: Where do we stand?. Indian J Soc Psychiatry 2017;33:69-70, doi: 10.4103/ijsp.ijsp_47_17, Available from:https://www.indjsp.org/text.asp?2017/33/2/69/209195.

Kallivayalil RA, Enara A. Mental health in an unequal world - The role of social determinants. Indian J Soc Psychiatry [serial online] 2022 [cited 2023 Feb 20];38:3-6. Available from: https://www.indjsp.org/text.asp?2022/38/1/3/341339.

Kawa I, Carter JD, Joyce PR, Doughty CJ, Frampton CM, Wells JE, Walsh AE, Olds RJ. Gender differences in bipolar disorder: age of onset, course, comorbidity, and symptom presentation. Bipolar Disord. 2005 Apr;7(2):119-25. doi: 10.1111/j.1399-5618.2004.00180.x. PMID: 15762852.

Kazan Kizilkurt, O., Giynas, F. E., Yazici Gulec, M., & Gulec, H. Bipolar disorder and perceived social support: Relation with clinical course, and the role of suicidal behaviour. Psychiatry and Clinical Psychopharmacology,2019; 29(4), 787–793. https://doi.org/10.1080/24750573.2019.1639410.

Kemner SM, van Haren NE, Bootsman F, Eijkemans MJ, Vonk R, van der Schot AC, Nolen WA, Hillegers MH. The influence of life events on first and recurrent admissions in bipolar disorder. Int J Bipolar Disord. 2015 Feb 25;3:6. doi: 10.1186/s40345-015-0022-4. PMID: 25717427; PMCID: PMC4339321.

Kennedy S, Thompson R, Stancer HC, Roy A, Persad E. Life events precipitating mania. Br J Psychiatry. 1983 Apr;142:398-403. doi: 10.1192/bjp.142.4.398. PMID: 6850179.

Khanna R, Gupta N, Shanker S. Course of bipolar disorder in eastern India. J Affect Disord. 1992 Jan;24(1):35-41. doi: 10.1016/0165-0327(92)90058-e. PMID: 1545043.

Kocalevent RD, Berg L, Beutel ME, Hinz A, Zenger M, Härter M, Nater U, Brähler E. Social support in the general population: standardization of the Oslo social support scale (OSSS-3). BMC Psychol. 2018 Jul 17;6(1):31. doi: 10.1186/s40359-018-0249-9. PMID: 30016997; PMCID: PMC6050647.

Kulhara P, Basu D, Mattoo SK, Sharan P, Chopra R. Lithium prophylaxis of recurrent bipolar affective disorder: long-term outcome and its psychosocial correlates. J Affect Disord. 1999 Jul;54(1-2):87-96. doi: 10.1016/s0165-0327(98)00145-1. PMID: 10403151.

Kumari A, Jahan M. Distressful life events in affective disorder. J Indian Acad Appl Psychol. 2006 Jul;32:193-200.

Lau BW, Lee JC, So K. Neurogenic hypothesis and psychiatric disorders. Chinese Science Bulletin. 2013 Sep;58(26):3188-98. doi: 10.1007/s11434-013- 5886-z.

Malkoff-Schwartz S, Frank E, Anderson BP, Hlastala SA, Luther JF, Sherrill JT, Houck PR, Kupfer DJ. Social rhythm disruption and stressful life events in the onset of bipolar and unipolar episodes. Psychol Med. 2000 Sep;30(5):1005-16. doi: 10.1017/s0033291799002706. PMID: 12027038.

Mathew BS, Thomas SP, & Kallivayalil, RA. Gender differences in bipolar disorder- a cross-sectional study in central Kerala. Kerala Journal of Psychiatry, 2022; 35(1), 1-8. https://doi.org/10.30834/KJP.35.1.2022.288.

McPherson H, Herbison P, Romans S. Life events and relapse in established bipolar affective disorder. Br J Psychiatry. 1993 Sep;163:381-5. doi: 10.1192/bjp.163.3.381. PMID: 8401970.

Merikangas KR, Akiskal HS, Angst J, Greenberg PE, Hirschfeld RM, Petukhova M, Kessler RC. Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. Arch Gen Psychiatry. 2007 May;64(5):543-52. doi: 10.1001/archpsyc.64.5.543. Erratum in: Arch Gen Psychiatry. 2007 Sep;64(9):1039. PMID: 17485606;

PMCID: PMC1931566.

Miasso AI, do Carmo BP, Tirapelli CR. Transtorno afetivo bipolar: perfil farmacoterapêutico e adesão ao medicamento [Bipolar affective disorder: pharmacotherapeutic profile and adherence to medication]. Rev Esc Enferm USP. 2012 Jun;46(3):689-95. Portuguese. doi: 10.1590/s0080-62342012000300022. PMID: 22773491.

Miklowitz DJ, Goldstein MJ, Nuechterlein KH, Snyder KS, Mintz J. Family factors and the course of bipolar affective disorder. Arch Gen Psychiatry. 1988 Mar;45(3):225-31. doi: 10.1001/archpsyc.1988.01800270033004. PMID: 3341878.

Narayanaswamy JC, Moily N, Kubendran S, Reddy YC, Jain S. Does latitude as a zeitgeber affect the course of bipolar affective disorder? Med Hypotheses. 2014 Sep;83(3):387-90. doi: 10.1016/j.mehy.2014.06.017. Epub 2014 Jun 25. PMID: 25066100.

Negash A, Alem A, Kebede D, Deyessa N, Shibre T, Kullgren G. Prevalence and clinical characteristics of bipolar I disorder in Butajira, Ethiopia: a community-based study. J Affect Disord. 2005 Aug;87(2-3):193-201. doi: 10.1016/j.jad.2005.03.011. PMID: 15913783.

Nisha A, Sathesh V, Punnoose VP, Varghese PJ. A comparative study on psycho-socio-demographic and clinical profile of patients with bipolar versus unipolar depression. Indian J Psychiatry. 2015 Oct-Dec;57(4):392-6. doi: 10.4103/0019-5545.171842. PMID: 26813699; PMCID: PMC4711241.

O'Connell RA, Mayo JA, Eng LK, Jones JS, Gabel RH. Social support and long-term lithium outcome. Br J Psychiatry. 1985 Sep;147:272-5. doi: 10.1192/bjp.147.3.272. PMID: 3933602.

Pardoen D, Bauwens F, Dramaix M, Tracy A, Genevrois C, Staner L, Mendlewicz J. Life events and primary affective disorders. A one year prospective study. Br J Psychiatry. 1996 Aug;169(2):160-6. doi: 10.1192/bjp.169.2.160. PMID: 8871791.

Perugi G, Micheli C, Akiskal HS, Madaro D, Socci C, Quilici C, Musetti L. Polarity of the first episode, clinical characteristics, and course of manic depressive illness: a systematic retrospective investigation of 320 bipolar I patients. Compr Psychiatry. 2000 Jan-Feb;41(1):13-8. doi: 10.1016/s0010-440x(00)90125-1. PMID: 10646613.

Pompili M, Harnic D, Gonda X, Forte A, Dominici G, Innamorati M, et al. Impact of living with bipolar patients: Making sense of caregivers' burden. World J Psychiatry. 2014 Mar 22;4(1):1-12. doi: 10.5498/wjp.v4.i1.1. PMID: 24660140; PMCID: PMC3958651.

Post RM, Leverich GS, Xing G, Weiss RB. Developmental vulnerabilities to the onset and course of bipolar disorder. Dev Psychopathol. 2001 Summer;13(3):581-98. doi: 10.1017/s0954579401003091. PMID: 11523849.

Post RM. Transduction of psychosocial stress into the neurobiology of recurrent affective disorder. Am J Psychiatry. 1992 Aug;149(8):999-1010. doi: 10.1176/ajp.149.8.999. PMID: 1353322.

Sagar R, Pattanayak RD. Potential biomarkers for bipolar disorder: Where do we stand? Indian J Med Res. 2017 Jan;145(1):7-16. doi: 10.4103/ijmr.IJMR_1386_16. PMID: 28574009; PMCID: PMC5460576.

Sam SP, Nisha A, Varghese PJ. Stressful Life Events and Relapse in Bipolar Affective Disorder: A Cross-Sectional Study from a Tertiary Care Center of Southern India. Indian J Psychol Med. 2019 Jan-Feb;41(1):61-67. doi: 10.4103/IJPSYM.IJPSYM_113_18. PMID: 30783310; PMCID: PMC6337920.

Selvakumar N, Menon V, Kattimani S. A Cross-sectional analysis of patterns and predictors of medication adherence in bipolar disorder: Single Center Experience from South India. Clin Psychopharmacol Neurosci. 2018 May 31;16(2):168-175. doi: 10.9758/cpn.2018.16.2.168. PMID: 29739130; PMCID: PMC5953016.

Shaik S, Rajkumar RP, Menon V, Sarkar S. Gender, life events, and depression: an exploratory study. Indian J Psychol Med. 2017 May-Jun;39(3):330-335. doi: 10.4103/0253-7176.207339. PMID: 28615769; PMCID: PMC5461845.

Simhandl C, Radua J, König B, Amann BL. The prevalence and effect of life events in 222 bipolar I and II patients: a prospective, naturalistic 4 year follow-up study. J Affect Disord. 2015 Jan 1;170:166-71. doi: 10.1016/j.jad.2014.08.043. Epub 2014 Sep 6. PMID: 25240845.

Singh G, Kaur D, Kaur H. Presumptive stressful life events scale (PSLES) – a new stressful life events scale for use in India. Indian J Psychiatry. 1984 Apr;26(2):107-14. PMID: 21965968; PMCID: PMC3012215.

Smoller JW, Finn CT. Family, twin, and adoption studies of bipolar disorder. Am J Med Genet C Semin Med Genet. 2003 Nov 15;123C(1):48-58. doi: 10.1002/ajmg.c.20013. PMID: 14601036.

Solomon DA, Leon AC, Coryell WH, Endicott J, Li C, Fiedorowicz JG, Boyken L, Keller MB. Longitudinal course of bipolar I disorder: duration of mood episodes. Arch Gen Psychiatry. 2010 Apr;67(4):339-47. doi: 10.1001/archgenpsychiatry.2010.15. PMID: 20368510; PMCID: PMC3677763.

Staner L, Tracy A, Dramaix M, Genevrois C, Vanderelst M, Vilane A, Bauwens F, Pardoen D, Mendlewicz J. Clinical and psychosocial predictors of recurrence in recovered bipolar and unipolar depressives: a one-year controlled prospective study. Psychiatry Res. 1997 Mar 3;69(1):39-51. doi: 10.1016/s0165-1781(96)03021-1. PMID: 9080544.

Subramanian K, Sarkar S, Kattimani S, Philip Rajkumar R, Penchilaiya V. Role of stressful life events and kindling in bipolar disorder: Converging evidence from a mania-predominant illness course. Psychiatry Res. 2017 Dec;258:434-437. doi: 10.1016/j.psychres.2017.08.073. Epub 2017 Aug 30. PMID: 28870645.

Subramanian K, Sarkar S, Kattimani S. Bipolar disorder in Asia: Illness course and contributing factors. Asian J Psychiatr. 2017 Oct;29:16-29. doi: 10.1016/j.ajp.2017.04.009. Epub 2017 Apr 19. PMID: 29061417.

Swendsen J, Hammen C, Heller T, Gitlin M. Correlates of stress reactivity in patients with bipolar disorder. Am J Psychiatry. 1995 May;152(5):795-7. doi: 10.1176/ajp.152.5.795. PMID: 7726323.

Weinstock LM, Miller IW. Psychosocial predictors of mood symptoms 1 year after acute phase treatment of bipolar I disorder. Compr Psychiatry. 2010 Sep-Oct;51(5):497-503. doi: 10.1016/j.comppsych.2010.02.001. Epub 2010 Mar 12. PMID: 20728007; PMCID: PMC2947345.

Wilkins K. Bipolar I disorder, social support and work. Health Rep.

2004;15 Suppl:21-30. PMID: 15748042.

World Health Organization. Adherence to long-term therapies: evidence for action. World Health Organization; 2003. Available at https://apps.who.int/iris/handle/10665/42682.

Yadav R, Kandre D. Stressful life events in bipolar mood disorder. Int J Res Med. 2016;5(2):109-14.

Young RC, Biggs JT, Ziegler VE, Meyer DA. A rating scale for mania: reliability, validity and sensitivity. Br J Psychiatry. 1978 Nov;133:429-35. doi: 10.1192/bjp.133.5.429. PMID: 728692.