

Original Research Article

Volume 13 Issue 3

March 2024

A CLINICAL STUDY TO EVALUATE THE EFFECTIVENESS OF INDIVIDUALIZED HOMOEOPATHIC MEDICINE IN REDUCING THE IRRITABILITY IN BIPOLAR I DISORDER – A STUDY PROTOCOL

¹Dr. M. Gnnanaprakasham*, ²Dr. Aiswarya J

¹Associate Professor (Dept. of Psychiatry), ²Junior Resident, (Dept. of Psychiatry)

Kerala University of Health Sciences, Thrissur

*Corresponding Author's Email ID: drgprakashpsy@gmail.com

ABSTRACT:

Objective: Bipolar Affective Disorder (BPAD), previously known as manic-depressive psychosis (MDP), characterized by unusual changes in mood, energy, activity levels and inability to carry out routine tasks. The symptoms were noticed in repeated (ie.atleast two) episodes of high or low mood at different times. Irritability is a psychological emotional response to a provoking stimulus, which can be seen both in manic and depressive episodes of bipolar disorder. This study aims to determine the effectiveness of individualized homoeopathic medicine in the reduction of irritability in patients diagnosed with Bipolar I Disorder. It also helps to understand the reduction in frequency of episodes and intensity of irritability in Bipolar I after using homoeopathic medicines.

Materials and Methods: The study design is Interventional Study-Before & After treatment without a control group. The patients who present with symptoms of irritability in Bipolar I disorder at Outpatient department, Inpatient Department and Peripheral Centers of NHRIMH Kottayam will be screened using screening form. The cases fulfilling inclusion and exclusion criteria's will be enrolled in the study after approval of Psychiatrist and patients consent. The trial sample size is calculated as 35 considering 15% dropouts. The period of enrollment and follow up shall be for 1 ½ years which includes 6 months enrollment and 1 year follow up. Cases will be assessed at the Baseline with Born Steiner Irritability scale (BSIS) to measure the irritability, and Scale for the Assessment of Episodes in Bipolar Disorder (SAEBD) is used for the intensity of symptoms of bipolar disorder. Each case will be reviewed at every 4 weeks interval with the Born Steiner Irritability scale (BSIS) till the conclusion of the study. SAEBD will be used to assess the cases at the Baseline and every three months till the conclusion of the study. The outcome of the study will be assessed by difference of scores obtained during baseline and end in BSIS scale, and SAEBD scale.

Discussion and Conclusion: Bipolar disorder stands out as one of the prominent conditions among the mental disorders. A recent study shows there is increase in diagnosis of BPAD at early onset which in turn result in poor prognosis. The need of early diagnosis and timely management call for immediate attention. Irritability is a symptom of both manic and depressive episodes of Bipolar 1 disorder. This clinical study provides a novel impression in the assessment and reduction of irritability in BPAD-I. It is also expected that the study helps in understanding the irritability which forms main precipitating factor in majority of cases and believed to reduce the intensity of irritability and frequency of episodes in Bipolar I disorder.

KEY WORDS: BPAD- 1, Irritability, Single arm clinical study, Homoeopathy

39

INTRODUCTION:

BACKGROUND AND RATIONALE:

Bipolar Affective Disorder (BPAD), previously known as manic-depressive psychosis (MDP), which causes unusual changes in mood, energy, activity levels and inability to carry out routine tasks. It is characterized by repeated (ie.atleast two) episodes of high or low mood at different times. Recovery is usually complete in between the episodes¹.According to DSM-V, one manic episode in a life time is required for the diagnosis of bipolar I disorder².Mania is the characteristic phase of bipolar disorder, and a significant contributor to cognitive decline, disabling conditions, and social stigma.³ The prevalence of bipolar disorder in the general population has been growing over the last decade. World Mental Health Survey estimates worldwide lifetime prevalence of 2.4% of bipolar spectrum disorders, in which 0.6% met criteria for bipolar I disorder,0.4% for bipolar II and 1.4% for subthreshold bipolar disorder. The most recent estimates from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) have reported substantially greater lifetime prevalence estimates of bipolar I disorder of 3.3, Bipolar II of 1.1 with corresponding 12 month rates of 2.0 and 0.8, respectively⁴. Males had a slightly higher rate for current prevalence of bipolar affective disorder (0.3%) when compared to females (0.2%), women have more depressive episodes and men have more manic episodes over lifetime. Bipolar affective disorder exhibited a higher prevalence among specific demographic groups. Individuals aged 40 to 49.9 years accounted for 0.4% of cases, while urban metro residents constituted 0.7% of the affected population⁵. According to the Global burden of Disease study in 2017, 7.6 million people had been diagnosed for bipolar disorder in India. All of the Indian states had a frequency that varied by a factor of 1.3, with Sikkim, Goa, Kerala and Himachal Pradesh having the greatest prevalence of any state⁶.

Patients with bipolar disorder have shown hyperactivity in amygdala and hypoactivity in hippocampus and prefrontal cortex which presents with impaired executive function and heightened emotions respectively. Among the biogenic amines, norepinephrine and serotonin are the two neurotransmitters most implicated in the underlying mechanism of mood disorders⁷.

Irritability is a symptom of both manic and depressive episodes in the DSM-V. Manic episodes usually involve a distinct period of abnormally and persistently elevated, expansive, or irritable mood, along with elevated energy, increased goal-directed activity, pressure of speech, distractibility, inflated self-esteem and decreased need for sleep, lasting for at least 1 week. Depressive episode presented as sadness, empty or irritable mood, loss of interest or pleasure, changes in weight, psychomotor agitation or retardation along with depressive ideation². Manic episodes usually last between 2 weeks and 4-5 months. But depression tends to last longer (median length about 6 months)¹.

Irritability is a psychological emotional response to a provoking stimulus, commonly seen in mental disorders such as generalized anxiety disorder, post-traumatic stress disorder, bipolar disorder, borderline personality disorder, and nicotine withdrawal⁸. Abnormal irritability is not only limited to mania, but also in depressive episodes of bipolar disorder¹³.

A study on 'Anxiety, Irritability and Agitation as indicators of bipolar mania with depressive symptoms' showed that 4.2% anxiety, 5.6% irritability, 10.3% agitation, and 15.7% both agitation and irritability in individuals with bipolar disorder.⁸

Bipolar population is differentially affected by several 'stress-sensitive' medical disorders, obesity and diabetes mellitus. Neurological disorders (e.g., migraine), respiratory disorder, infectious diseases are also prevalent with substance-use disorders¹⁰. Stigmatisation of sick patients renders them helpless and socially isolated¹¹.

In the conventional mode of treatment, the most commonly used pharmacologic therapies are mood stabilizers, atypical antipsychotics, and antidepressants, which cause serious side effects. Homoeopathy an effective alternative mode of treatment brings speedy recovery without any drug side effects.

Recent studies have revealed a significant increase in the contribution of mental disorders to India's overall disease burden, doubling from 1990 to 2017. Among these mental disorders, bipolar disorder stands out as one of the prominent conditions⁶. Irritability was observed in 62.4% of individuals diagnosed with bipolar disorder⁹. Bipolar disorder exhibits a higher prevalence during adolescence, experiences a substantial increase in adulthood, and shows a modest decline in old age. These trends underscore the imperative to explore a broader range of treatment options tailored to the varying stages of prevalence¹².

There is no cure for bipolar disorder, but treatment can help to control symptoms and reduce repetition of episodes with regards to the mood changes and behavioral problems. Studies shows no specific treatment for cases of irritability but which may respond to a range of treatments in conventional pharmacotherapy¹³. Long-term use of these medicines may have some adverse effects.

In a case series by Bernardo Merizalde showed the effectiveness of individualized homoeopathic medicine as a main therapeutic approach in bipolar disorder¹⁴. They were also given supportive and insight-oriented psychotherapy and were minimally provided conventional medicine.

Miriam Wheeler¹⁵ in her case report on treatment of bipolar disorder by platinum metallicum showed the effectiveness of homoeopathy in improvement of symptoms with no relapses in episodes.

Karunakara Moorthi¹⁶ in a case report prescribed Lachesis mutus 200 and then Lycopodium clavatum 200 in a 55-year male patient with mania in bipolar disorder with overall improvement without support of any conventional medicine.

Studies on Homeopathic management in symptoms of bipolar disorder have shown that Homoeopathic medicines are capable of reducing intensity of symptoms in a short period. There was no study conducted in Homoeopathy to know the reduction of irritability which forms the main underlying cause and precipitating factor during an episode of illness.

This study is aimed to explore the possibilities of Individualized Homoeopathy in the management of Irritability in Bipolar 1 disorders.

MATERIALS AND METHODS:

It is an Interventional Study-Before & After treatment without a control group. The sample size has been calculated as 35 considering 15% dropouts. The patients will be enrolled from Outpatient department, Inpatient Department and Peripheral Centers of

National Homoeopathy Research Institute in Mental Health, Kottayam, Kerala, India.

This clinical trial adheres to the latest revision of the Helsinki Declaration on human experimentation and Good Clinical Practices of India. The protocol has been designed following the guidance provided by Institutional Review Board. The finalized protocol has been subjected to Institutional Ethical Committee approval. Further review of the protocol and final approval from the university has been obtained. The CTRI registration number is CTRI/2024/01/061059.

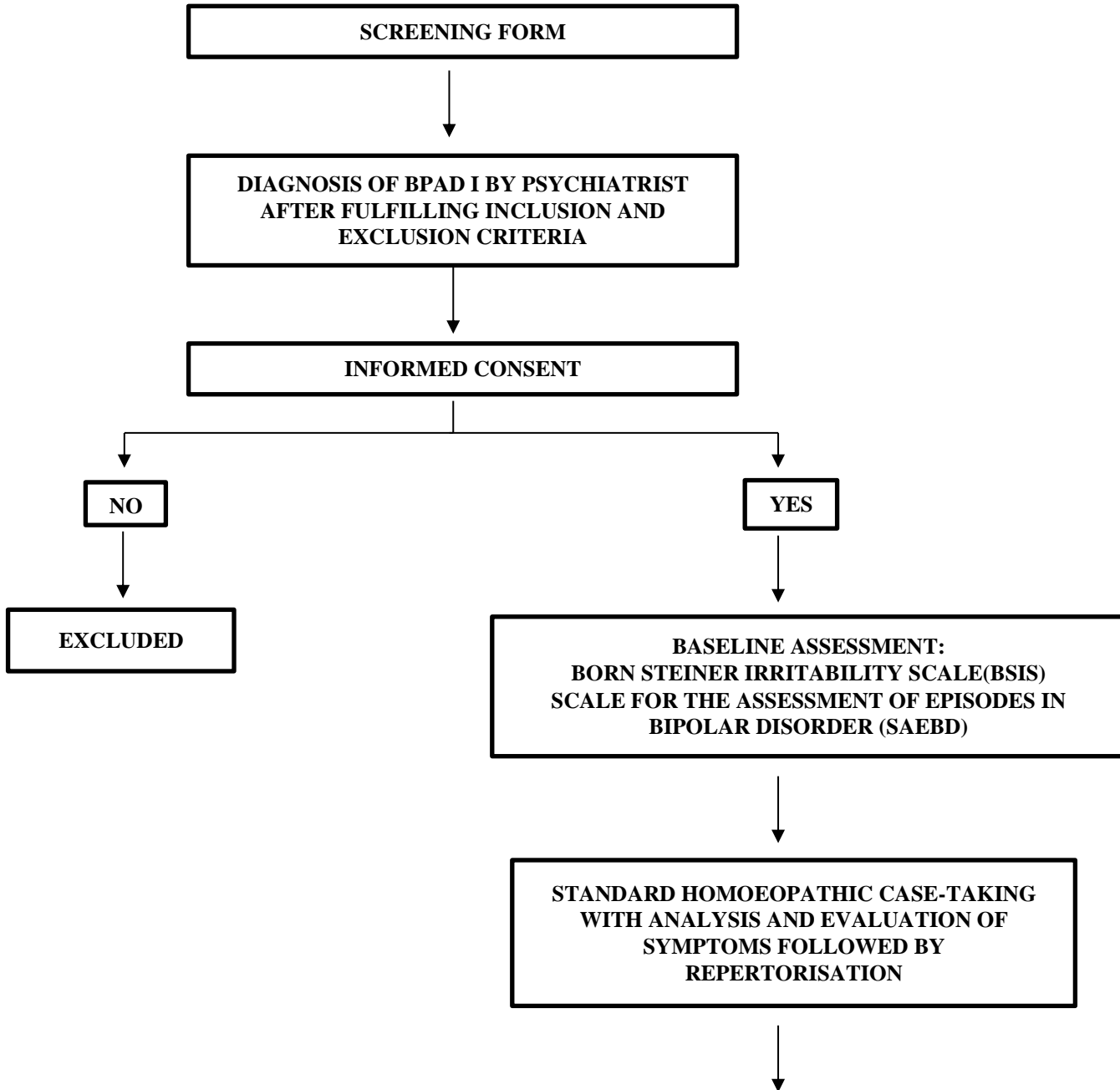
SCREENING AND ENROLLMENT:

The patients presenting with symptoms of irritability in Bipolar I disorder at Outpatient department, Inpatient Department and Peripheral Centers of NHRIMH will be screened using screening form. The cases fulfilling inclusion and exclusion criteria will be enrolled for the study. A copy of patient Information sheet will be given to the parent/ caretaker after explaining the details of the study. The Informed consent form will be obtained from parents or caretaker based on the availability. Detailed case taking will be done in the standard Homoeopathic case record format prepared for the study.

INCLUSION CRITERIA:

Ages from 18 to 65 years, both sexes who have fulfilled the DSM-V criteria for Bipolar 1 disorder, with or without psychotic symptoms will be included in the study after getting the consent.

The Flowchart of complete study (Figure 1):



**HOMOEOPATHIC INTERVENTION AFTER
MATERIA MEDICA REFERENCE**



FOLLOW UP ASSESSMENT:

- 1. BORN STEINER IRRITABILITY SCALE (BSIS) FOR ASSESSING IRRITABILITY IN EVERY MONTH TILL THE END OF THE STUDY.**
- 2. SYMPTOMS OF BIPOLAR 1 DISORDER ASSESSED WITH SCALE FOR THE ASSESSMENT OF EPISODES IN BIPOLAR DISORDER (SAEBD), AT EVERY THREE MONTHS TILL THE END OF THE STUDY.**
- 3. HOMOEOPATHIC INTERVENTION FORM WILL BE ASSESSED EVERY MONTH, SCHEDULED/ UNSCHEDULED FOLLOW – UPS**

INTERVENTION:

Detailed case taking will be done in the case record format prepared for the study. Totality of the symptoms shall be constituted after analysis and evaluation of the complete case. The symptoms will be repertorized using the suitable repertory in RADAR Opus software and the final selection of remedy will be done after consulting with standard Homoeopathic Materia Medica. The indicated medicines will be started in the centesimal potency and shall be increased as per the requirement of the case. The dose and repetition will be based on the Homoeopathic principles. If the improvement stops the potency of the medicine will be raised. If there is no change, the case will be re-analyzed and another appropriate Homoeopathic remedy will be administered. In case of any acute complaints, the acute totality will be erected and appropriate remedy will be administered and data will be analyzed separately. The Homoeopathic management part will be practiced adhering strict standard operative procedures of Homoeopathic Principles. Homoeopathic assessment will be done on every month using homoeopathic intervention format prepared for the study.

FOLLOW – UP:

Participants in the study will undergo comprehensive monitoring, with monthly follow-up assessments documented on a chart. Upon initial enrollment, each patient will receive a follow-up calendar outlining visit dates for the entire year. The chart incorporates details such as follow-up dates, times, and scheduled measures for the 12-month duration. A regular telephonic and other available communications will be done via mail, telephonic calls by social worker to maintain a good compliance.

DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS FIFTH EDITION (DSM-5) CRITERIA FOR BIPOLAR 1 DISORDER

The manic episode may have been preceded by and may be followed by hypomanic or major depressive episodes. At least one lifetime manic episode is required for the diagnosis of bipolar I disorder.

Manic Episode

The diagnostic criteria for a manic episode include a distinct period of abnormally elevated mood and increased energy lasting at least one week, with specific symptoms such as inflated self-esteem, decreased need for sleep, and heightened goal-directed activity.

Hypomanic Episode: Hypomanic episodes, while common in bipolar I disorder, are not obligatory for its diagnosis, involving a distinct period of abnormally elevated mood lasting at least four consecutive days.

Major Depressive Episode

For a major depressive episode, five or more symptoms, including depressed mood or loss of interest, persist for at least two weeks, causing significant distress or impairment; these symptoms are not attributed to substance use or another medical condition, and while common in bipolar I disorder, a major depressive episode is not mandatory for its diagnosis.

OUTCOME MEASURES:

Outcome of treatment will be assessed according to difference in scores of BSIS scale done at the Baseline and every month till the conclusion of the study, to analyse the frequency of repetition of episodes and intensity of irritability in subsequent episodes of Bipolar 1 disorder. Also assessed in accordance with difference in scores of SAEBD scale to find out reduction of symptoms of Bipolar 1 disorder which will be used at the Baseline and every three months till the conclusion of the study.

Primary outcome:

Reduction in irritability with improvement in BSIS scale score

Secondary outcome:

1. Evaluating the reduction in frequency of episodes of irritability in Bipolar 1 disorder assessed using Born Steiner Irritability scale (BSIS).
2. Evaluating the reduction in intensity of irritability in subsequent episodes of Bipolar 1 disorder assessed using Born Steiner Irritability scale (BSIS).
3. Evaluating the reduction of symptoms of Bipolar 1 disorder will be assessed using Scale for the Assessment of Episodes in Bipolar Disorder (SAEBD).

CRITERIA FOR BASELINE AND FOLLOW – UP ASSESSMENT:

Cases will be assessed at the baseline with Born Steiner Irritability scale (BSIS), and Scale for the Assessment of Episodes in Bipolar Disorder (SAEBD). Subsequently Born Steiner Irritability scale (BSIS) will be assessed every month till the conclusion of the study. Scale for the Assessment of Episodes in Bipolar Disorder (SAEBD) will be used to assess the cases at the Baseline and every three months till the end of the study. Homoeopathic assessment will be done on every month using homoeopathic intervention format prepared for the study.

DATA COLLECTION: Standardized case recording format and predesigned excel sheet shall be used for the data capturing. The diagnostic information gathered through the assessment of cases using Born Steiner Irritability scale (BSIS), and Scale for the Assessment of Episodes in Bipolar Disorder (SAEBD) at the baseline. Follow-up information will be gathered through the timely assessment of each cases using scales. The outcome of treatment will be assessed according to BSIS, follow-up charts and SAEBD scale.

TIMELINE OF THE STUDY:

Time	Study Period						Closeout
	Enrolment	Post allocation in month					
		3	6	9	12	Every month	
Eligibility screening	+	-	-	-	-	-	-
Informed consent	+	-	-	-	-	-	-
Interventions Homoeopathy	+	+	+	+	+	+	+
Born Steiner Irritability scale (BSIS)	+	+	+	+	+	+	+
Scale for the Assessment of Episodes in Bipolar Disorder (SAEBD)	+	+	+	+	+	-	+

SAMPLE SIZE:

Since there are no previous study conducted in irritability, Homoeopathy and BPAD, there were no data available. Therefore, sample size of 30 was selected. Considering 15% dropout, 35 cases may be enrolled.

STATISTICAL ANALYSIS:

Data will be analyzed using suitable software. Descriptive analysis will be done for demographic variables. The normality of the data will be checked. The changes in Born Steiner Irritability scale (BSIS) and Scale for the Assessment of Episodes in Bipolar Disorder (SAEBD) total score at baseline and end will be compared using paired t-test based on normality of data.

DISCUSSION AND CONCLUSION:

Homeopathy holds significance as a therapeutic approach due to its holistic nature, considering physical, mental, and emotional symptoms to select similimum. There is a lack of existing studies on the treatment of irritability in bipolar I disorder. Long-term use of conventional pharmacotherapy may have some adverse effects. Studies on Homeopathic management in symptoms of bipolar disorder have shown that Homoeopathic medicines are capable of reducing intensity of symptoms in a short period.

This study aims to investigate the potential of Individualized Homeopathy in effectively managing irritability in bipolar I disorder. Beyond its primary goal, the research seeks to establish a robust foundation and introduce a novel perspective on comprehending the efficacy of homeopathic medicine through a symptom-based approach within a specific diagnosis. The study not only contributes valuable insights into the management of irritability in bipolar I disorder but also promotes the advancement of research methodologies. By emphasizing a symptom-based psychopathological understanding in the prescription process, the study encourages the exploration of innovative avenues for future research in the field of homeopathy and mental health.

ACKNOWLEDGEMENT:

I Acknowledge Dr.K.C. Muraleedharan Officer in charge, Dr.R. Sitharthan, Principal, and all other faculties of NHRIMH for their support and encouragement at all times. I also Acknowledge reviewers of Kerala University of Health sciences, Thrissur for critical review of my research proposal and helped me to extend my knowledge.

CONFLICT OF INTEREST:

The author declares that there is no conflict of interest.

REFERENCES:

1. World Health Organization. The ICD-10 Classifications of Mental and Behavioural Disorder: Clinical Descriptions and Diagnostic Guidelines. Geneva:
2. World Health Organization; 1993.
3. American Psychiatry Association. The Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Arlington DC: American Psychiatric Association; 2013.
4. Niraj Ahuja. A short textbook of psychiatry. New Delhi, India: Jaypee Brothers Medical Publishers; 2011.
5. Shah N, Grover S, Rao GP. Clinical practice guidelines for management of bipolar disorder. Indian Journal of Psychiatry. 2019 ;59(5):51.
6. Sadock BJ, Verduin ML, Ruiz P, Arya Shah. Kaplan & Sadock's Synopsis of Psychiatry. 12th ed. Philadelphia: Wolters Kluwer; 2022.
7. Sagar R, Dandona R, Gururaj G, Dhaliwal RS, Singh A, Ferrari A, Dua T, Ganguli A, Varghese M, Chakma JK, Kumar GA. The burden of mental disorders across the states of India: The Global Burden of Disease Study. 1990–2017. The Lancet Psychiatry. 2020 Feb 1;7(2):148-61.
8. Manji HK, Quiroz JA, Payne JL, Singh J, Lopes BP, Viegas JS, Zarate CA. The underlying neurobiology of bipolar disorder, World Psychiatry. 2003 oct; 2(3):136.

9. Safer DJ. Irritable mood and the Diagnostic and Statistical Manual of Mental Disorders. *Child and Adolescent Psychiatry and Mental Health*. 2009 Oct 24;3(1).
10. Suppes T, Eberhard J, Lemming O, Young AH, McIntyre RS. Anxiety, irritability, and agitation as indicators of bipolar mania with depressive symptoms: a post hoc analysis of two clinical trials. *International Journal of Bipolar Disorders*. 2017 Nov 6;5(1).
11. Deckersbach T, Perlis RH, Frankle WG, Gray SM, Grandin L, Dougherty DD, et al. Presence of Irritability During Depressive Episodes in Bipolar Disorder. *CNS Spectrums*. 2004 Mar;9(3):227–31.
12. McIntyre RS, Soczynska JK, Beyer JL, Woldeyohannes HO, Law CW, Miranda A, Konarski JZ, Kennedy SH. Medical comorbidity in bipolar disorder: reprioritizing 10 unmet needs. *Current Opinion in Psychiatry*. 2007 Jul 1;20(4):406-16.
13. Ranjbar M, SeyedFatemi N, MardaniHamooleh M, Esmaeeli N, Haghani SH. Correlation of Stigma with Self-compassion in Patients with Bipolar Disorder. *Iran Journal of Nursing*. 2020 Feb;32(122):1-3.
14. Vidal-Ribas P, Brotman MA, Valdivieso I, Leibenluft E, Stringaris A. The Status of Irritability in Psychiatry: A Conceptual and Quantitative Review. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2016 Jul;55(7):556–Merizalde B. Bipolar Disorders: A Presentation of Three Cases. *American Journal of Homeopathic Medicine*. 2004; 96:300-15.
15. Wheeler M, Oskin J, Langland J. Alternating Symptoms in the Homoeopathic Treatment of Bipolar Disorder. *Platinum Metallicum: A Case Report*. *American Journal of Homeopathic Medicine*. 2015 Dec 1;108(4). 11
16. Moorthi S, Radhika P, Muraleedharan K. Usefulness of individualised homoeopathic medicine in Manic episode - A case report. *Indian J Res Homoeopathy* 2021;15(1):41-47. doi: 10.4103/ijrh.ijrh-25-20