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Study of reasons for relapse in patients with bipolar I disorder with repeat admissions and its correlation with substance use

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ABSTRACT

Background: Mood disorder is one of the common causes, for which psychiatric consultations are sought. A better understanding of the factors that lead to repeated admissions, increased relapse rates, and concurrent substance dependence is necessary for the development of interventions that may reduce the likelihood of adverse effects in patient with bipolar I disorder. **Aims and Objectives:** The aims of this study were as follows: (1) To study the correlation between the reasons for relapse and substance use with various sociodemographic factors in patients having bipolar I disorders and (2) to find out the correlation between reasons for relapse, substance use, and severity of illness. **Materials and Methods:** This was a cross-sectional single interview study, in which 67 consecutive patients having bipolar I disorder and admitted in psychiatry ward were admitted on the basis of a pre-defined inclusion and exclusion criteria. The details about psychiatric, relapse-related symptoms, substance use-related symptoms, as well as other aspects of clinical profile were taken. **Results:** Out of 67 patients, 51 (76.1%) were male and 16 (23.8%) were female. Mean age of the participants was 30.43 years (S.D. = 9.05). Sleep disturbance was seen in all patients (67) and was also the most common symptom. It was followed by psychomotor disturbances in 60 (89.5%) of the patients. Among 67 patients included in the study, substance use was seen among 28 (41.7%) of the patients. Substance use was significantly associated with age of the patients and occupation (P = 0.03 each). The age group of more than 30 years (57.7%) had significantly higher substance use compared to those < 30 years (31.7%). **Conclusion:** Concurrent substance use is associated with increased risk of relapse and readmissions in cases of patients with bipolar I disorders. A thorough history is necessary to rule out substance use in these cases.

Key words: Bipolar I disorder; Readmissions; Relapse; Substance use

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INTRODUCTION

Mood disorders are considered syndromes consisting of a cluster of signs and symptoms, sustained over a period of weeks to months that represent a marked departure from a person's habitual functioning and tend to recur, often in periodic or cyclical fashion. Bipolar I disorder includes at least one manic episode or occurrence of episode of mania and major depressive disorder which is not better explained by other psychiatric disorder involving affective features.[1]

National mental health survey showed a lifetime prevalence of 1.4% for Schizophrenia and psychotic disorders and 5.6% for mood disorders. The lifetime prevalence of depressive disorders was 5.1% and was nearly double the current prevalence rate (2.7%).[2] The current rates for schizophrenia and other psychotic disorders were about one-fourth of the lifetime prevalence indicating the chronicity of the disorder.[3] Life time incidence of bipolar I disorder in the general population is approximately 1%. Episode of mania is characterized by elated mood and

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increased activity level, in which a person feels decreased need for sleep, talks excessively, grandiose thoughts, excessive money spending, uninterrupted speech, and hypersexuality, whereas depressive episode is characterized by sadness of mood, decreased interest in surroundings, slowness of activity, low self-esteem, reduced concentration span, and disturbed sleep.[4]

It has been found in the studies that the relapse rates in bipolar I disorder patient are around 39–52% per year, in spite of the regular treatment.[5] In majority of these patients, minimum two acute mood episodes occur and most of them show multiple recurrences of affective symptoms. Relapse of symptoms in bipolar I disorder patients may be associated with natural traits, that is, affective temperament which includes anxious, depressive, irritable traits, and other traits also. Seasonal variation leading to relapse of symptoms and therefore repeated admissions in these patients is many a time gender specific and may show variable symptoms than usual presentation.[6]

Hence, the better understanding of the factors leading to relapse and repeated admission in these patients is warranted, and recently, this has become the main area of research. Substance use is commonly associated with bipolar mood disorder and both these conditions are associated with poor psychosocial health, cognitive, and memory deficits also.[7] Substance use in patient with bipolar mood disorder may lead to, increased number of repeat admissions, relapse may alter the efficacy of mood stabilizers and thus its effect. Substance use in these patients may also increase the severity of depressive features with increase in the tendency of suicidal attempts in these patients.[8] Concomitant substance use disorder in these patients represents high clinical burden and has adverse effect on further outcome and treatment response, so these patients may require better psychosocial education and newer treatment approach.[9] Thus, a better understanding of the factors that lead to repeated admissions, increased relapse rates, and concurrent substance dependence is necessary for the development of interventions that may reduce the likelihood of adverse effects in patient with bipolar I disorder.[10]

With this background in mind, the present study will focus on factors causing relapse, repeated admissions, and its correlation with substance use in patients of bipolar I disorder admitted in psychiatry ward.

Aims and objectives

The objective of this study were as follows:

1. To study the correlation between the reasons for relapse and substance use with various sociodemographic factors in patients having bipolar I disorders
2. To find out the correlation between reasons for relapse, substance use, and severity of illness.

MATERIALS AND METHODS

This was a cross-sectional single interview study, in which 67 consecutive patients having bipolar I disorder and admitted in psychiatry ward were admitted on the basis of a predefined inclusion and exclusion criteria. The study protocol was approved by the Institutional Ethics Committee. Keeping power (1-beta error) at 80% and confidence interval (1-alpha error) at 95%, the minimum sample size required in each group was 50 patients; therefore, we included 67 (more than minimum required number of cases) specimens in this study. After taking written informed consent, data information was collected along the specialized pro forma prepared for the study. The details about psychiatric, relapse-related symptoms, substance use-related symptoms, as well as other aspects of clinical profile were taken. The diagnosis was made as per the DSM-V (Annexure-II) and ICD 10 criteria (Annexure-Ill). Each participant was individually interviewed with Brief Psychiatry Rating Scale (BPRS), Young's Mania Rating scale (YMRS), Hamilton Rating Scale for Depression (HAM-D), and Relapse questionnaire.

Confidentiality of data was strictly maintained. Privacy was maintained while undertaking the interview. All data thus collected were tabulated and analyzed statistically using SSPS 21.0 software. $P<0.05$ was taken as statistically significant.

Inclusion criteria

The following criteria were included in the study:

- Patients of bipolar I disorder admitted in psychiatry ward
- Patient aged between 18 years and 60 years
- Caretaker willing to participate and give written informed consent.

Exclusion criteria

The following criteria were excluded from the study:

- Caretaker not willing to give consent for participation
- Patients with other major comorbid medical, surgical or psychiatric conditions.

RESULTS

Mean age of the participants was 30.43 years (S.D.=9.05). Among all the patients included in the study, most common age group was 20–30 years 37 (55.22%) followed by 30–40 years 19 (28.36%), 40–50 years 7 (10.45%), and 50–60 years patients were 4 (5.97%). Gender distribution

of the patients showed out of 67 patients, 51 (76.1%) were male and 16 (23.8%) were female. In terms of occupational status, 43 (64.2%) if the patients were employed and 24 (35.8%) of them were unemployed. Thirty (44.8%) of the participants were married and 37 (55.2%) were unmarried. Among the study subjects, 36 (53.7%) were from rural residential background, while 31 (46.3%) were residing in urban areas. Out of 67 participants, 43 (64.2%) of the participants were educated up to more than secondary levels, while 24 (35.8%) were educated up to secondary levels (Table 1).

Among studied cases, 56 (83.6%) were diagnosed with bipolar I disorder most recent episode mania, whereas 11 (16.4%) were diagnosed with bipolar I disorder most recent episode depression. Among all the patients, sleep disturbance was seen in all patients (67) and was also the most common symptom. The sleep disturbance was common during manic as well as depressive episode as it was seen in all patients (56 and 11 patients). It was followed by psychomotor disturbances in 60 (89.5%) of the patients, followed by excessive talking with talking big and mood elation seen among 56 (83.6%) patients, psychotic features were seen in 56 (83.6%), hyperreligiosity was seen among 45 (67.16%) of the patient population. The aggressive behavior was seen among 34 (50.7%), suspiciousness in 32 (47.7%) spending spree in 28 (41.7%). The least common symptoms were fatigue, sadness of mood, anhedonia, guilt feeling, decreased concentration, suicidal thoughts, and significant weight loss 10 (14.9%), 11 (16.4%), 10 (14.9%), 6 (8.9%), 11 (16.4%), 6 (8.9%), and 1(1.49%), respectively (Figure 1).

Psychotic features were seen in 56 (83.58%) patients. Among 67 patients included in the study, substance use was seen among 28 (41.7%) of the patients. The most common substance used was nicotine (in form of tobacco chewing) among 13 (46.4%) patients, followed by alcohol and nicotine together among eight patients (28.6 %), alcohol, nicotine, and cannabis together in 4 (14.3), and only alcohol in 3 (10.7%) patients. Clinical profile, past history, family history, personal history, and premorbid personality were assessed using standard questionnaire. Each patient was also assessed for mental status (Table 2).

Mental status examination of all the patients revealed that all the patients were cooperative, 24 (35.8%) of the them were excessively groomed. Attention was arousable and sustained in 47 (70.14%) of the patients. The eye-to-eye contact was initiated and maintained in all the patients and rapport was also established with all of them. The mood was elated in 50 (74.6%) of the patients and sad among 11 (16.4%) of the patients. Affect was congruent to mood among 58 (86.5%) of the patients. The speech

Table 1: Demographic details of the studied cases

Demographic factors	Frequency (n=67)	Percentage
Age group (years)		
20–29	37	55.22
30–39	19	28.36
40–49	7	10.45
50–59	4	5.97
Mean Age=30.43±9.05 years		
Gender		
Male	51	76.1
Female	16	23.8
Occupational Status		
Employed	43	64.2
Unemployed	24	35.8
Marital status		
Married	30	44.8
Unmarried	37	55.2
Residential Background		
Urban	31	46.3
Rural	36	53.7
Educational Status		
Up to secondary	24	35.8
>Secondary	43	64.2

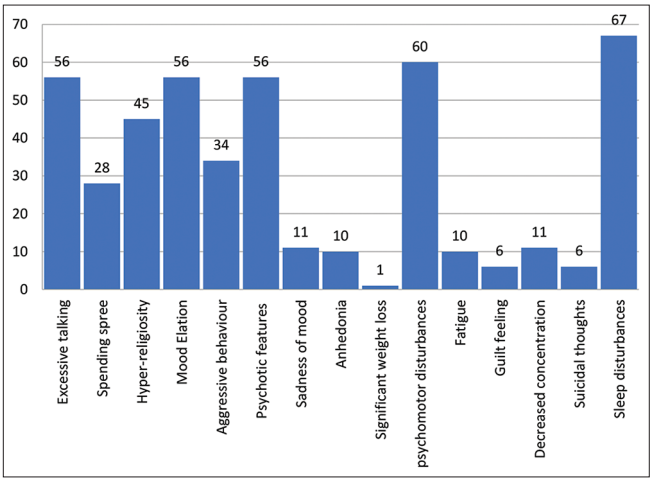

Figure 1: Clinical presentation of the studied cases

was pressured among 23 (34.3%) of the patients. In thought, idea/delusion of grandiosity was present among 47 (70.1%) of the patients, idea/delusion of grandiosity with persecution was present among 9 (13.4%) of patients, ideas of helplessness, hopelessness, and worthlessness (HHW) were present among 8 (11.9%), and ideas of HHW along with delusion of guilt were present among 3 (4.47%) of the patients. No patient had perceptual abnormality. All the patients were well oriented. The memory was impaired among 26 (38.8%) of the patients, judgment was impaired among 45(67.2%), and concept was impaired among 22 (32.8%). Sixteen (23.9%) patients had Grade A insight, Grade B in 24(35.8%), and Grade C in 27 (40.2%) patients.

Clinical diagnosis of all the patients (n=67) revealed, 56 (83.6%) were diagnosed with bipolar I disorder most

recent episode mania, whereas 11 (16.4%) were diagnosed with bipolar I disorder most recent episode depression. Participants diagnosed with bipolar I disorder mania were assessed for the severity of manic symptoms using YMRS which revealed that severe mania was seen among 25 (44.6%) of the patients and moderate mania among 29 (51.8%) of the patients, and 2 (3.57%) had mild mania. Assessment of participants diagnosed as bipolar I disorder – depression for the severity of their symptoms using HAM-D revealed that 6 (54.5%) of the patients were having very severe depressive symptoms and 5 (45.5%) of the patient had severe depressive symptoms (Table 3).

The assessment of correlation of demographic factors with non-compliance due to irregular medication consumption revealed that there was no significant correlation of age,

Table 2: Substance abuse, clinical profile, and history of the studied cases

Substance use and clinical profile	Profile	Frequency (n=28)	Percentage
Substance			
Type of substance	Alcohol	3	10.7
	Nicotine	13	46.4
	Alcohol+nicotine	8	28.6
	Alcohol+nicotine+cannabis	4	14.3
Duration of substance use (years)	<5	6	21.4
	5–10	11	39.2
	>10	11	39.2
Substance Consumption increased since	15 days–1 month	9	32.1
	1 month–6 months	13	46.4
	>6months	6	21.4
Dependence pattern	Present	27	96.4
	Absent	1	3.57
Withdrawal symptoms	Present	9	32.1
	Absent	19	67.9
Clinical profile – and history			
Number of previous mood episodes	1–3	17	25.4
	>3	50	74.6
Number of previous admissions	1–2	41	61.2
	>2	26	38.8
H/O deliberate self-harm attempt	Present	23	34.3
	Absent	44	65.6
Family History of bipolar disorders	Present	26	38.8
	Absent	41	61.1
Premorbid personality	Cluster A traits	3	4.5
	Cluster B traits	34	50.7
	Cluster C traits	10	14.9
	No specific cluster traits	20	29.8

Table 3: Diagnosis and severity of bipolar I disorder in studied cases

Diagnosis and Severity	No of cases	Percentage
Clinical Diagnosis		
Bipolar I Disorder – Mania	56	83.6
Bipolar I disorder – Depression	11	16.4
Bipolar affective disorder most recent episode mania with psychotic symptoms	32	47.76
Bipolar affective disorder most recent episode mania without psychotic symptoms	24	35.82
DSM-5 Diagnosis		
Bipolar I disorder most recent episode manic with mood congruent psychotic features	47	70.14
Bipolar I disorder most recent episode manic with mood incongruent psychotic Features	9	13.43
Bipolar I disorder most recent episode depression	11	16.41
YMSR Severity		
Minimal Symptoms (13–19)	0	0
Mild Mania (20–25)	2	3.57
Moderate Mania (26–37)	29	51.8
Severe Mania (38–60)	25	44.6
HAM-D severity		
Mild (8–13)	0	0
Moderate (14–18)	0	0
Severe (19–22)	5	45.5
Very Severe (>23)	6	54.5

HAM-D: Hamilton rating scale for depression

gender, occupation, residential background, and marital status with non-compliance due to irregular medication consumption (Chi-square P values 0.1,0.8, 0.2, 0.6, and 0.2, respectively). There was significant correlation of educational status with non-compliance due to poor medication adherence (P=0.02). There was significantly higher proportion of non-compliance among the participants who were educated till secondary school (i.e., 87.5%) compared to those who were educated up to more than secondary (i.e., 39.53%).

The assessment of correlation of demographic factors with non-compliance due to side effects of medication revealed that there was no significant correlation of age, gender, residential background, and marital status with side effects to medicines (Chi-square P-values 0.2, 0.5, 0.7, and 0.7, respectively). There was significant correlation of educational status and occupation with non-compliance due to side effect of medicine (P=0.05 each). There was significantly higher proportion of non-compliance among the participants who were educated till secondary school (i.e., 83.3%) compared to those who were educated up to more than secondary (i.e., 60.4) and also significantly higher proportion of non-compliance was seen among the participants who were unemployed (i.e., 83.3%) compared to those who were employed (i.e., 60.4%) (Table 4).

The correlation of demographic factors with spontaneous relapse revealed that there was no significant correlation between age, gender, residential background, and marital status with spontaneous relapse without any reason (Chi-square P-value 0.7, 0.8, 0.1, and 0.2, respectively). Occupation and education were significantly associated with spontaneous relapses (P-value 0.01 and 0.05, respectively).

Table 4: Correlation of non-compliance due to irregular medicine consumption and side effects with sociodemographic factors

Factors	n=67	Compliant to medications	Non-compliant to medications	χ^2	P-value
Correlation of Non-compliance due to irregular medicine consumption and sociodemographic factors					
Age (years)					
<30 years	41	15	26	2.28	0.13
>30 years	26	5	21		
Gender					
Male	51	15	36	0.02	0.8
Female	16	5	11		
Occupation					
Unemployed	24	5	19	1.45	0.2
Employed	43	15	28		
Education					
Secondary	24	3	21	5.37	0.02
>Secondary	43	17	26		
Residential background					
Rural	36	10	26	0.15	0.6
Urban	31	10	21		
Marital Status					
Married	30	7	23	1.10	0.2
Unmarried	37	13	24		
Correlation of non-compliance due to side effects with socio- demographic factors					
Age (years)					
<30 years	41	26	15	1.34	0.2
>30 years	26	20	6		
Gender					
Male	51	36	15	1.37	0.54
Female	16	10	6		
Occupation					
Unemployed	24	20	4	3.47	0.05
Employed	43	26	17		
Education					
Secondary	24	20	4	3.47	0.05
>Secondary	43	26	17		
Residential background					
Rural	36	24	12	0.14	0.7
Urban	31	22	9		
Marital Status					
Married	30	20	10	0.1	0.7
Unmarried	37	26	11		
Unmarried	37	11	26		

There was significantly higher spontaneous relapse among the employed patients (i.e., 46.5%) as compared to those not employed i.e. (i.e., 16.7%). Furthermore, significantly higher spontaneous relapse was seen among patients who were educated up to more than secondary (i.e., 44.2%) as compared to those educated till secondary (i.e., 20.8%) (Table 5).

The assessment was done for correlation of sleep disturbances related to relapse with demographic factors. There were no significant associations found among different categories of demographic variables with age, gender, occupation, education, residential background, and marital status (Chi-square P-values 0.9, 0.3, 0.8, 0.1, 0.08, and 0.8, respectively). Relapse related to seasonal variation was significantly associated with different age group, residential back ground, and marital status (P<0.01 for each).

Relapse related to seasonal variation was significantly high with age group of more than 30 years (i.e., 61.5%) as compared to those <30 years (i.e., 17%). Among the patients with different residential back ground, rural patients had significantly higher relapse related to seasonal variation (i.e., 52.8%) as compared to urban patients (i.e., 12.9%). Married patients (i.e., 63.3%) had significantly higher relapse related to seasonal variation as compared to unmarried patients (i.e., 10.8%). Assessment of seasonal variations related to relapse with number of previous admissions revealed that both these factors were significantly correlated. Participants who had relapse related to season had significantly higher number of previous admissions (Chi-square P<0.01) as compared to those without it. Assessment of family history of bipolar I disorder and number of previous mood episodes revealed that both these factors were significantly correlated. Participants who had family history of bipolar I disorder had significantly higher number of previous mood episodes (Chi-square P=0.03) as compared to those without it.

Substance use was significantly associated with age of the patients and occupation (P=0.03 each). The age group of more than 30 years (57.7%) had significantly higher substance use compared to those <30 years (31.7%). Employed patients (51.2%) had significantly higher substance use than unemployed patients (25%). Substance use was significantly associated with age of the patients and occupation (P values 0.03 each). The age group of more than 30 years (57.7%) had significantly higher substance use compared to those <30 years (31.7%). Employed patients (51.2%) had significantly higher substance use than unemployed patients (25%). The substance use was not significantly associated with education, residential background, and marital status (P-value 0.6, 0.6, and 0.08, respectively). Assessment of premorbid personality and substance use among the participants revealed that both these factors were significantly correlated.

There was no significant correlation of substance use with any of the reasons associated with relapse, namely, non-compliance due to irregular medications, presence of stressor, spontaneous relapse, sleep disturbances, and seasonal variation (Chi-square test P-value 0.06, 0.07, 0.6, 0.4, and 0.4, respectively). Reasons related to relapse and substance use among participants was correlated with severity of illness using BPRS revealed that there was significant correlation between presence of stressor and severity of illness. There was no significant correlation between, any of the reasons related to relapse, namely, non-compliance due to irregular medications, sleep disturbances, seasonal variation, spontaneous relapse, increased substance use, and severity of illness. (Chi-square P-value 0.3, 0.7, 0.9, 0.5, and 0.6, respectively).

Table 5: Correlation of sociodemographic factors with spontaneous relapse

Factors	n=67	Spontaneous relapse	Non-spontaneous Relapse	χ^2	P-value
Age (years)					
<30 years	41	14	27	0.12	0.7
>30 years	26	10	16		
Gender					
Male	51	18	33	0.02	0.8
Female	16	6	10		
Occupation					
Unemployed	24	4	20	5.96	0.01
Employed	43	20	23		
Education					
Secondary	24	6	19	3.65	0.05
>Secondary	43	19	24		
Residential background					
Rural	36	16	20	2.51	0.1
Urban	31	8	23		
Marital Status					
Married	30	13	17	1.31	0.2
Unmarried	37	11	26		

Reasons related to relapse and substance use among participants with diagnosis of bipolar I disorder- mania was correlated with severity of illness using YMRS which revealed that there was no significant correlation between, any of the reasons related to relapse, namely, non-compliance due to irregular medications, presence of stressor, sleep disturbances, seasonal variation, spontaneous relapse, increased substance use, and severity of illness (Chi-square P-value 0.5, 0.8, 0.1, 0.5, 0.3, and 0.1, respectively).

Reasons related to relapse and substance use among participants with diagnosis of bipolar I disorder – depression was correlated with severity of illness using HAMD which revealed that there was no significant correlation between, any of the reasons related to relapse, namely, non-compliance due to irregular medications, sleep disturbances, seasonal variation, spontaneous relapse, increased substance use, and severity of illness (Chi-square P-value 0.7, 0.8, 0.6, 0.3, and 0.7, respectively).

DISCUSSION

In our study, the maximum number of study subjects belonged to younger age group, that is, <30 years, with the range of age between 20 years and 60 years and majority of them were male (76%). Various studies have shown similar findings of male presenting more with manic illness than females. Similar age and gender distribution was observed in a work by Gania et al.,[11] Manning et al., studied 837 patients with particular concern with the problem of gambling and substance use in patients attending community health clinics in Australia. The mean age of the studied cases was found to be 38±13 years.[12]

In the present study, more than half of the participants, that is, 43 (64.2) was employed that this finding was consistent with study by Saddichha et al.[13] Majority of the participants were unmarried as most participants were from age group of 20–30 years, about 44.8% were married. The relationship between marital status and mood disorders is very complex. Being single or divorced/separated is either a risk factor for mood disorder or the consequence of the negative life events generated by depressive and/or manic states. In the present study, about more than half of the participants were educated up to more than secondary and 35.8% were educated up to secondary level. This could be due to the fact that comparatively higher educated people have more help seeking behaviour.[14] Similar finding were seen in study done by Tondo et al., concluded that recurrence rates (episodes/year) and proportion of time in mania were highest (with more manias/year) in BD-I subjects.[15]

In our study, suicidal thoughts were present in a small number of patients (8.95%). The studied conducted by Swann et al.,[16] and Isometsä,[17] reported that predominantly depressive course of illness was found to have a 2-fold risk of suicide attempts, compared with predominantly manic patients; including patients with mixed states into depressive polarity strengthens the association to 4.5-fold.

In our study, substance use was seen among 28 (41.7%) of the participants. Nicotine (in the form of Chewable tobacco) alone was the most common substance used (46.4%), followed by nicotine in combination with alcohol (28.6%) followed by alcohol, nicotine, and cannabis together (14.3%). In a study by Luciano et al., smoking tobacco was the commonest substance of abuse followed by Alcohol, Cannabis, Amphetamines, and Sedatives and Nicotine and alcohol addiction usually coexisted among the study participants and similar finding was seen in our study. There was no significant difference between the mean HAMD scores of the participants with respect to non-compliance, sleep disturbance, seasonal variations, and spontaneous relapse and Substance use. (P-value 0.7, 0.8, 0.6, 0.3, and 0.7).

Luciano et al. stated in their study that three successful relapse prevention strategies emerged from their data: Building a supportive community, participating in active versus passive activities, and maintaining a healthy attitude.[18] Similar findings were also reported by the authors such as Tolliver and Anton[19] and Kessing et al.[20]

Limitation of the study

In our study, majority of the patients were male and this male preponderance may be due to reluctance on the part of family members to seek psychiatric help for female patients. Reasons for relapse could be different in female participants which demands separate study. Furthermore, a multicentric study with relatively large number of patients would further conclusive findings.

CONCLUSION

This study showed that there are multiple reasons leading to relapse of symptoms in bipolar I disorders and concurrent substance use increases the risk of relapse. Early identification of reasons related to relapse and early intervention during follow-up assessment can help in reducing the repeated admissions in patients of bipolar I disorders.

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REFERENCES

1. Marvel CL and Paradiso S. Cognitive and neurological impairment in mood disorders. Psychiatr Clin North Am. 2004;27(1):19-36.
   https://doi.org/10.1016/S0193-953X(03)00106-0
2. Murthy RS. National mental health survey of India 2015-2016. Indian J Psychiatry. 2017;59(1):21-26.
   https://doi.org/10.4103/psychiatry.IndianJPsychiatry_102_17
3. Saha S, Chant D, Welham J and McGrath J. A systematic review of the prevalence of schizophrenia. PLoS Med. 2005;2(5):e141.
   https://doi.org/10.1371/journal.pmed.0020141
4. Culpepper L. The diagnosis and treatment of bipolar disorder: Decision-making in primary care. Prim Care Companion CNS Disord. 2014;16(3):PCC.13r01609.
   https://doi.org/10.4088/PCC.13r01609
5. Perlis RH, Ostacher MJ, Patel JK, Marangell LB, Zhang H, Wisniewski SR, et al. Predictors of recurrence in bipolar disorder: Primary outcomes from the systematic treatment enhancement program for bipolar disorder (STEP-BD). Am J Psychiatry. 2006;163(2):217-224.
   https://doi.org/10.1176/appi.ajp.163.2.217
6. Geoffroy PA, Bellivier F, Scott J, Boudebesse C, Lajnef M, Garad S, et al. Bipolar disorder with seasonal pattern: Clinical characteristics and gender influences. Chronobiol Int. 2013;30(9):1101-1107.
   https://doi.org/10.3109/07420528.2013.800091
7. Post RM and Kalivas P. Bipolar disorder and substance misuse: Pathological and therapeutic implications of their comorbidity and cross-sensitisation. Br J Psychiatry. 2013;202(3):172-176.
   https://doi.org/10.1192/bjp.bp.112.116855
8. Sublette ME, Carballo JJ, Moreno C, Galfalvy HC, Brent DA, Birmaher B, et al. Substance use disorders and suicide attempts in bipolar subtypes. J Psychiatr Res. 2009;43(3):230-238.
   https://doi.org/10.1016/j.jpsychires.2008.05.001
9. Jhanjee S. Evidence based psychosocial interventions in substance use. Indian J Psychol Med. 2014;36(2):112-118.
   https://doi.org/10.4103/0253-7176.130960
10. Lagerberg TV, Icick R, Aminoff SR, Nerhus M, Barrett EA, Bjella TD, et al. Substance misuse trajectories and risk of relapse in the early course of bipolar disorder. Front Psychiatry. 2021;12:656912.
    https://doi.org/10.3389/fpsyt.2021.656912
11. Gania A, Margoob M, Shah H, Khan AW, Ghosh A and Basu D. Psychiatric comorbidity in patients with substance use disorder: A hospital-based study. Indian J Soc Psychiatry. 2017;33(1):63-66.
    https://doi.org/10.4103/0971-9962.200093
12. Manning V, Dowling NA, Lee S, Rodda S, Garfield JB, Volberg R, et al. Problem gambling and substance use in patients attending community mental health services. J Behav Addict. 2017;6(4):678-688.
    https://doi.org/10.1556/2006.6.2017.077
13. Saddichha S, Prakash R, Sinha BN and Khess CR. Perceived reasons for and consequences of substance abuse among patients with psychosis. Prim Care Companion J Clin Psychiatry. 2010;12(5):PCC.09m00926.
    https://doi.org/10.4088/PCC.09m00926gry
14. Ramdurg S and Kumar S. Study of socio-demographic profile, phenomenology, course and outcome of bipolar disorder in Indian population. Int J Health Allied Sci. 2013;2(4):260-263.
    https://doi.org/10.4103/2278-344X.126729
15. Tondo L, Vazquez GH and Baldessarini RJ. Depression and mania in bipolar disorder. Curr Neuropharmacol. 2017;15(3):353-358.
    https://doi.org/10.2174/1570159X14666160606210811
16. Swann AC, Lijffijt M, Lane SD, Steinberg JL and Moeller FG. Interactions between bipolar disorder and antisocial personality disorder in trait impulsivity and severity of illness. Acta Psychiatr Scand. 2010;121(6):453-461.
    https://doi.org/10.1111/j.1600-0447.2009.01528.x
17. Isometsä E. Suicidal behaviour in mood disorders-who, when, and why? Can J Psychiatry. 2014;59(3):120-130.
    https://doi.org/10.1177/070674371405900303
18. Luciano A, Bryan EL, Carpenter-Song EA, Woods M, Armstrong K and Drake RE. Long-term sobriety strategies for men with co-occurring disorders. J Dual Diagn. 2014;10(4):212-219.
    https://doi.org/10.1080/15504263.2014.961884
19. Tolliver BK and Anton RF. Assessment and treatment of mood disorders in the context of substance abuse. Dialogues Clin Neurosci. 2015;17(2):181-190.
    https://doi.org/10.31887/DCNS.2015.17.2/btolliver
20. Kessing LV, Hansen MG, Andersen PK, Angst J. The predictive effect of episodes on the risk of recurrence in depressive and bipolar disorders a life-long perspective. Acta Psychiatr Scand. 2004;109(5):339-344.
    https://doi.org/10.1046/j.1600-0447.2003.00266.x

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MM- Concept and design of the study; interpreted the results, prepared first draft of manuscript and critical revision of the manuscript; **AS-** Design of the study, Statistically analyzed and interpreted; reviewed the literature and manuscript preparation; **AS-** Revision of the manuscript, Concept and coordination of the overall study; **VK-** Design of the study and revision of the manuscript

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