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Original Research Article

Study of clinical profile of patients of bipolar mood disorder with and without substance abuse and clinical course variables in the substance abusing bipolar group in one of the tertiary care centre of North India

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ABSTRACT

Background: Bipolar disorder is the sixth leading cause of disability worldwide and has a lifetime prevalence of about 3% in general population. In patients with bipolar disorder there was 58 % lifetime prevalence of co-occurring alcohol abuse and a 38 % lifetime prevalence of co-occurring other substance abuse. Substance abuse interferes with treatment and management approaches of the bipolar disorder.
Methods: A cross sectional observational study of 120 male patients divided in substance abusing (60) and non-substance abusing groups (60) with bipolar disorder according to DSM-V, who met the Inclusion criteria . A written informed consent was obtained from the patients and/ or their family members. Patient's information was recorded on the socio-demographic and clinical profile sheet .Thereafter, YMRS or HAM-D scales were applied as per the phase of the illness.
Results: Most of the patients were between 15-25 years in SAB group and 35-50 years in NSAB group, educated, semiskilled and married. Tobacco abuse was the commonest followed by cannabis and alcohol abuse. The mean duration of hospital stay in SAB group was 41.40 days and in NSAB group was 43.20 days. Dysphoric mania, aggressive behavior and suicidal attempts were more in SAB group. Mean total YMRS score of SAB group was greater than NSAB group.
Conclusions: Maximum patients had onset of substance abuse before the onset of affective symptoms. Manic symptomatology was more severe in substance abusing group.

Keywords: Affective symptoms, Bipolar disorder, Substance abuse

INTRODUCTION

Bipolar affective disorder is the sixth leading cause of disability worldwide and has a lifetime prevalence of about 3% in general population.[1] According to DSM-V Bipolar is characterized by occurrence of one or more manic episodes or manic episodes with depressive episodes. Episodes of substance induced mood disorder or of mood disorders due to general medical condition do not count towards a diagnosis of bipolar disorder.[2]

DSM-V defines substance abuse as a maladaptive pattern of substance use manifested by recurrent significant adverse consequences related to repeated failure to fulfill major role of obligations, repeated use in situations in which it is physically hazardous, multiple legal problems, and recurrent social and interpersonal problems. The essential feature of substance dependence is a cluster of cognitive, behavioral and physiological symptoms indicating that the individual continues use of substance despite significant substance related problems.[3]

Substance abuse is common during the course of bipolar disorder. National Institute of Mental health (NIMH) Epidemiological Catchment Area (ECA) study has found that over 60% patients with Bipolar disorder developed substance abuse disorder during life time.[4] These patients have often been referred to as dual diagnosis patients and treated as a separate group of patients since the treatment strategies are quite different from non-substance abusing patients. The relationship of the two or more disorders in the comorbid condition is intricate and in many clinical situations it is difficult to analyze. These cases can be categorized into many groups based on the drug abuse, the nature of psychiatric symptomatology and the etiological significance. Broadly, without getting into the finer aspects of etiological debate, these patients can be categorized into the following four groups:

Primary substance use disorder with secondary psychiatric disorder

The occurrence of depression in many cases of alcoholism has been seen as being caused by the secondary psychological and social effects of alcohol.[5]

Primary psychiatric disorder with secondary substance use disorder

Mood disorder leading to a pattern of use of any substance that may amount to abuse and schizophrenia contributing to cannabis abuse are the other examples.[5]

Primary psychiatric disorder with substance use disorder as part of the clinical syndrome

Nearly one third of the patients of mood disorder, in the depressive or the manic phase, are prone to escalate their substance use to an extent that they meet the criteria for dependence. This is also commonly seen in axis II diagnosis of personality disorders, in which the substance use is an epiphenomenon of the psychiatric disorder.[5]

Two primary coexisting disorders

Earlier it was believed that it was necessary to differentiate into primary and secondary disorders in cases of co-morbidity. It is now well recognized that two disorders can co-exist without one having led or contributed significantly towards the other. Common etiological basis had earlier been hypothesized for some of the co-morbid conditions like depression and alcoholism.[6] These elevated rates of substance abuse do not simply reflect the effect of chronic mental illness, since rates of substance abuse are elevated in bipolar patients even at the time of their first manic episodes. Recent studies show that bipolar illness initiates substance abuse either as an attempt at self-medication or as a direct result of affective symptoms. The substance abuse may initiate affective episodes through behavioral sensitization or kindling mechanism.[7]

There are contradictory reports from different studies regarding family history, age of onset of affective symptoms and the effects of substance abuse on clinical features of bipolar disorder. These differences may be due to the fact that these are conducted in different population across the globe.[8-11] These studies are likely to improve this understanding, with regards to the relationships between substance abuse and bipolar disorder and helps us in understanding treatment and management approaches for patients with both conditions. In view of the above mentioned facts, the current study was planned. As far as authors are aware, very few studies have been conducted in the past in the States of the Northern India. So this study was conducted in one of the Tertiary Care Hospital of North India after getting through the Ethical Committee approval.

Aims and objectives is to study the clinical profile of the patients of Bipolar Mood Disorder with and without substance abuse, to compare the substance abusing Bipolar patients and non-abusing Bipolar patients group on demographic variables and to study some clinical course variable of the substance abusing bipolar patients .

METHODS

Study was a cross sectional observational study. The sample was obtained from the patients attending the in-patient unit of the Department of Psychiatry in one of the tertiary care hospitals of North India from January 2016 to December 2016. The sample comprised of two groups. First group comprised of 60 male patients of Bipolar 1 disorder with substance abuse (Substance Abusing Bipolar - SAB group) fulfilling DSM-V criteria both for Bipolar 1 disorder and substance abuse. Second group comprised of 60 male patients of Bipolar 1 disorder without substance abuse (Non Substance Abusing Bipolar - NSAB group) fulfilling DSM-V criteria for Bipolar 1 disorder but not for substance abuse (except for Nicotine).

Inclusion criteria

- Male patients within the age range of 15-50 years.
- All patients of both groups fulfilling DSM-V criteria for Bipolar 1 Mood Disorder.
- Patients fulfilling DSM-V criteria for substance abuse or Patients of SAB group included those who were having affective symptoms either preceding substance abuse or in whom affective symptoms persisted after at least two weeks of substance free State.

Exclusion criteria

- Patients having substance induced mood disorders.
- Patients having severe physical or organic mental disorder.

- Patients having Intellectual disability.
- Patients not willing to give consent.

Socio demographic profile of the patients was recorded on a self-designed semi structured proforma which includes age, education, occupation, marital status, family structure and locality. The scale devised by Kuppuswamy et al, was used to determine Socio-economic Status.[12] A self-designed semi-structured performa was used to record the history and clinical details of the patients, including age of onset of affective symptoms, number of hospitalizations, duration of stay and presence of mixed episodes, dysphoric mania, rapid cycling, psychotic features, aggressive behavior and suicide attempts.

Young Mania Rating Scale (YMRS) is most frequently used rating scale to assess the severity of manic symptoms. It consists of a check list of 11 items. It is based on patient's subjective report of his or her clinical condition over the previous 48 hours. The total score ranges from 0 to 60.[13] Reliability is good, based on interpreter reliability and internal consistency studies. Validity is good, based on correlation with other mania measures.[14]

Hamilton Rating Scale for Depression (HAM-D) was developed by M Hamilton (1960), is the most widely utilized rating scale to assess symptoms of depression, with a focus on somatic symptomatology. Items on the HAM-D are scored 0 to 2 or 0 to 4 with total score on the 17- item version ranging from 0 to 50. Scores of 7 or less may be considered normal, 8 to 13 is mild, 14 to 18 is moderate, 19 to 22 is severe, and 23 or above is very severe depression . Reliability is good to excellent, including internal consistency and interpreter assessments. Validity is good based on correlation with other depression symptom measures.[15]

Patients of Bipolar disorder diagnosed as per DSM-V criteria, who met the inclusion criteria were included in the study. A written informed consent was obtained from the patients and/or their family members. Patient's information was recorded on the socio-demographic and clinical profile sheet. Detailed history was obtained from the patient and/or their family members followed by Physical and Mental Status Examination of the patients. Thereafter, YMRS /or HAM-D scales were applied as per the phase of the illness.

Statistical analysis

Descriptive statistics, in terms of percentage were used to describe the categorical variables.Mean and standard deviation were used to describe various characteristics related to continuous variables. Comparison between substance abusing and non-abusing bipolar patients was done by applying student's t test to continuous variables and Chi-square test to categorical variables. Yates' correction for chi-square test was applied wherever applicable.

RESULTS

Socio-demographic profile

Maximum number (43%) of patients in SAB group were within 15-25 years whereas (50%) in NSAB group were within 36-50 years of age range. About 63% of the patients in NSAB group and half 50% of the patients in SAB group were educated above metric. More than half of the patients were married in both groups. Nearly one third of patients in both groups (30% in SAB and 33.3% in NSAB) were semi/ unskilled workers followed by students (30% each) in both groups. Out of 60 patients in each group 38 patients in SAB group and 36 patients in NSAB group belong to lower middle socioeconomic status. Maximum number of patients in both the groups, 40 patients (66.7%) in SAB group and 50 patients (83%) in NSAB group living in nuclear families. Nearly (80%) of patients from both groups belonged to rural background (Table 1).

Clinical variables

Type of substance abuse in SAB group

Many patients in SAB group were abusing more than one substance. Tobacco abuse was the commonest (63.3%) followed by cannabis (60%) and alcohol (50%) abuse respectively (Table 2).

Age of onset of affective symptoms

The mean age of onset of affective symptoms in SAB group and NSAB group was 25.07 years; SD=7.061 and 27.50 years; SD 8.713, respectively.

Number of hospitalization and duration of hospital stay

The number of hospitalizations in SAB group was 2.17 (mean); SD=1.859 and in NSAB group it was 2.07 (mean); SD=2.167. The difference between number of hospitalizations among two groups was statistically insignificant ($t=0.192$; $p>0.1$). The mean duration of hospital stay in SAB group was 41.40 days and in NSAB group it was 43.20 days.

Specified clinical variables in SAB and NSAB groups

History of dysphoric mania, aggressive behavior and suicidal attempts was more in SAB group as compared to NSAB group. Presence of Mixed episode was more seen in NSAB group as compared to SAB group of patients (Table 3).

Course of illness

Change in quantity of substance intake in different phases of illness

During manic phase majority of patients increased and during depressive phase, nearly half of the patients revealed no change in the amount of the substance used (Table 4).

Table 1: Socio demographic profile.

Socio demographic profile		SAB GROUP No of patients (percentage)	NSAB GROUP No of patients (percentage)
AGE (in years)	15-25	26 (43%)	18 (30%)
	26-35	14 (23%)	12(20%)
	36-45	16 (27%)	16 (26%)
	46-50	4 (7%)	14 (24%)
Locality	Rural	48 (80%)	45(75%)
	Urban	12 (20%)	15 (25%)
Education	No formal schooling	10 (17%)	4 (7%)
	Up to primary	12 (20%)	12 (20%)
	Up to matriculation	8 (13%)	6(10%)
	Above metric	30 (50%)	38 (63%)
Occupation	Professional / semiprofessional	-	2 (3%)
	Clerk, shopkeeper, farmer, skilled worker	8 (13%)	4 (7%)
	Semi / unskilled	18 (30%)	20 (33%)
	Unemployed	16 (27%)	16 (27%)
	Student	18 (30%)	18 (30%)
Family Structure	Nuclear	40 (67%)	50 (83%)
	Joint	20 (33%)	10 (17%)
Marital status	Unmarried	28 (47%)	24 (40%)
	Married	32 (53%)	36 (60%)
Socioeconomic status (Kuppuswamy's scale)	Upper	-	-
	Upper middle	2 (3%)	4 (6%)
	Lower middle	38 (64%)	36 (60%)
	Upper lower	20 (33%)	20 (33%)
	Lower	-	-

Table 2: Type of substance abuse/dependence in SAB group (N=60).

Type of substance used	No. of patients*	%
Alcohol	30	50
Opioids	6	10
Cannabis	36	60
Tobacco	38	63.3
Sedatives	-	-
Others	-	-
Multiple	2	3.3

***** Some patients were abusing more than one substance

Relationship between the onset of substance abuse and onset of affective symptoms in SAB group

In 58 (96.66%) patients, onset of substance abuse started before the onset of affective symptoms and only in two patients (3.3%) affective symptoms started before substance abuse.

Comparison of YMRS scores of SAB group and NSAB group

Mean total YMRS score (27) of SAB group was greater than total YMRS score (24.33) of NSAB group. Sleep and Insight sub-score was significantly better (Table 5).

Comparison between HAM-D scores of SAB group and NSAB group

HAM-D sub scores on items 'Work and Activity' and 'Somatic symptoms- General' of SAB group patients were significantly higher than NSAB group of patients (Table 6).

DISCUSSION

Drugs abuse have long been recognized to interfere with diagnosis and treatment of major psychiatric disorders. In recent years the relationship between various psychiatric disorders and substance abuse has received increased

attention. Substance abuse is exceptionally common during the course of bipolar disorder.[16]

In India, alcohol and cannabis are more abused than LSD, Cocaine or Amphetamine, so the impact of substance abuse may be different in Indian population. The effect of substance abuse on bipolar disorder in Indian population has not been well studied.[17] Only male cases were taken because substance abuse in females is very less in North India.

Inclusion of female cases would have resulted in more female cases in non-substance abusing group and no or very few female cases in substance abusing group which could have led to a potential bias for comparison of two groups.[18]

Table 3: Comparison of some Specified clinical variables in the study groups.

Specified clinical variable	SAB group (N=60)		NSAB group (N=60)	
	No. of patients	Percentage	No. of patients	Percentage
Presence of mixed episodes	3	5	20	33.30
Presence of dysphoric Mania	40	66.70	36	60
Presence of rapid cyclic	6	10	2	3.30
Presence of psychotic features	48	80.00	50	83.30
Presence of aggressive behaviour	58	96.70	40	66.70
Presence of suicidal attempts	16	26.70	8	13.30

Table 4: Change in the quantity of substance used in different phases of illness in SAB group (N=60).

Quantity of the substance used	Mania		Depression		Intervening normal phase	
	No. of patients	%	No. of patients	%	No. of patients	%
Increase	46	76.70	20	33.30	2	3.30
Decrease	8	13.30	12	20.00	32	53.30
No change	6	10	28	46.60	26	43.30

Table 5: Comparison of YMRS scores of SAB group and NSAB group.

YMRS item	SAB		NSAB		p value
	Mean	SD	Mean	SD	
Elevated mood	1.93	0.781	1.92	1.139	0.132
Increased motor activity - energy	2.33	1.038	2.29	1.083	0.973
Sexual interest	1.15	0.770	0.75	0.608	0.889
Sleep	2.59	1.083	2.17	1.308	0.048*
Irritability	2.93	1.639	2.67	1.633	0.210
Speech (rate and amount)	3.67	1.387	3.75	1.700	0.575
Language -thought disorder	1.33	.832	1.17	0.702	0.848
Content	3.89	2.359	3.08	2.041	0.446
Disruptive-aggressive disorder	2.33	1.687	1.75	1.595	0.201
Appearance	1.30	0.669	0.83	0.565	0.212
Insight	3.74	0.813	3.88	0.448	0.011*
YMRS total score	27		24.33		

*p value significant at p<0.05

Sociodemographic variables

In the present study socio-demographic variables were comparable and did not significantly differ between SAB and NSAB group. Some of the previous studies Starkowaski and Del Bello also showed similar findings with regard to socio-demographic profile where no significant difference between patients with a lifetime history of drug abuse and those without drug abuse.

Some studies by Winokur et al, and Verdoux H revealed that the patients presenting with substance abuse were younger (nearly 20 years) than those without substance abuse like in the current study (in 15-25 years of age group). In a study by Morrison JR, socio-demographic factors did not differ except average age at the time of current admission which was significantly more around 40 years of age in Bipolar patients with substance abuse.[10,19,20]

In another study by Sonne et al, socio-demographic characteristics were similar to this study except for education. They found that non-abuser group had significantly more years of education as compared to substance abuser group of bipolar patients whereas in this study both groups (SAB and NSAB) were educated upto the same level.[21] Some of the previous studies from the West (Morrison JR, Sonne et al, and Tsai SY had been reported that 49%-74% of their patients were unmarried or living alone which is in contrast to this study where more than half of the patients were married.[20-22] The discrepancy noticed between the present study and those from the West may be due to different ethnic groups being studied. More number of patients (58.6%) were unemployed in both groups in some of the previous studies Sonne SC and Del Bello MP et al, as compared to this study where one third patients were semiskilled and one third patients were students.[7,23] This might be attributable to a higher level of tolerance of illness in this society.

Table 6: Comparison between HAM-D scores of SAB group and NSAB group.

HAM-D item	SAB		NSAB		p value
	Mean	SD	Mean	SD	
Depressed mood	2.00	1.000	1.17	0.753	0.491
Feeling of guilt	0.67	0.577	0.83	1.169	0.199
Suicide	1.00	1.732	0.17	0.408	0.826
Insomnia early	2.00	0.000	1.33	0.516	0.272
Insomnia middle	0.67	0.577	0.83	0.753	0.068
Insomnia late	2.00	0.000	0.83	0.408	0.749
Work and activity	3.00	1.000	2.83	1.602	0.002*
Retardation	0.33	0.577	1.17	0.983	0.876
Agitation	0.67	0.577	0.33	0.516	0.225
Anxiety psychic	2.00	1.000	1.50	0.837	0.407
Anxiety somatic	2.00	1.000	1.33	1.033	0.451
Somatic symptoms- gastrointestinal	0.00	0.000	1.00	0.632	0.388
Somatic symptoms - general	1.33	0.577	0.83	0.408	0.033*
Genital symptoms	1.00	1.000	1.00	0.894	0.170
Hypochondriasis	1.33	1.528	0.83	0.983	1.000
Loss of weight	1.00	1.000	1.00	0.632	0.563
Insight	0.67	1.155	1.50	0.548	1.000
Diurnal variation; A	1.00	1.000	1.00	0.632	0.170
Diurnal variation; B	0.67	0.577	0.67	0.516	1.000
Depersonalization and Derealization	1.00	1.000	0.17	0.408	1.000
Paranoid symptoms	0.33	0.577	0.67	0.816	0.106
Obsession and compulsive symptoms	1.00	1.000	0.50	0.837	0.553
HAM-D total score	25.67		21.50		

*p value significant at $p<0.05$

Clinical variables

Tobacco (63.3%) was the most commonly abused substance followed by Cannabis (60%) and Alcohol (50%) in SAB group patients. Opioid abuse was seen only in 10% of patients and just one patient was having multiple substance abuse. Most of the patients with Alcohol or Cannabis abusers were also dependent on Tobacco. In a Western study by Mueser et al, it was observed that after alcohol (66%), the common substances of abuse were cocaine (29%), cannabis (22%), amphetamine (21%), sedatives (20%) followed by hallucinogens and narcotics (10% each) among substance abusing bipolar patients.[24] This variation across populations can be explained on the basis of socio-cultural differences.

This study revealed that the mean age of onset of affective symptoms in SAB group was 25.07 years (SD=7.061) while in NSAB group it was 27.50 years (SD=8.713). The difference in the age of onset of affective symptoms in two groups was not statistically significant in this study similar to the study done by Escamilla MA et al.[9] Several studies Feinman JA and Dunner DL, Pini S et al, on the other hand reported that the age of onset of mood symptoms for substance abusers was significantly earlier than that of the non-substance abusers.[9,25,26]

In contrast, the difference in age of onset of affective symptoms in two groups was statistically significant in studies by Strakowski who found that patients hospitalized with first episode mania and antecedent alcohol use disorder had a significant later age of onset (mean age 27 years) than those without alcoholism (mean age 21 years).[27] Also in some of the earlier studies done by Morison JR and Del Bello MP et al, revealed that affective illness started at age around 23 years in non-substance abusing bipolar patients but not until around 28 years in substance abusing bipolar patients.[8,22] Thus the results regarding age of onset of affective symptoms in two groups are conflicting across various studies.

While comparing number of hospitalizations and duration of hospital stay in SAB and NSAB groups, similar to this finding, in some of the previous studies, number of hospitalizations did not significantly differ between patients with a lifetime history of drug abuse and those without.[10,19] Several other studies reported increased hospitalizations in bipolar patients with substance abuse.[21,28,29,30] One of the reasons for such difference could be due to the difference in severity of patients at the time of admission across various studies.

In this study, mixed states were more common in NSAB group whereas SAB group had more of dysphoric symptoms. In some of the earlier studies, substance abusing bipolar patients had more frequent mixed states.[28,31-33] Episodes of Aggressive behaviour (96.7%) and Suicide attempts (26.7%) were more prevalent in SAB patients as compared to NSAB patients in whom aggressive behaviour was found in 66.7% and suicide attempts in 13.3% patients. Potash BJ et al, and Brady KT also observed that a lifetime co-morbid substance use disorder was a significant predictor of suicide attempts.[34,35] This finding was similar to this study in which suicide attempts were higher in SAB group.

Clinical variables like rapid cycling and psychotic features were more common in SAB patients similar to some of the previous studies done by Escamilla MA et al, and Himmelhoch JM et al.[9,28] They also found that substance abusing bipolar patients had more dysphoric and irritable mood state, which also match this finding. They also found significant increase in rapid cycling, psychotic features, aggressive behaviour and suicidal attempts in substance abusing group.

Course of illness

Majority (76.7%) of the substance abusing bipolar patients increased the amount of substance abuse during manic phase of their illness. In several previous studies also, there was a trend towards higher rate of drug abuse during manic phase of illness. Three fourth of patients increased the amount of substance abuse during manic phase in this study whereas about one third of the patients increased the substance abuse in previous studies (Frey MA et al, and Sachdeva JS et al.[13,36] This could be explained by increased pleasure seeking behaviour during manic phase leading to increase in substance abuse and may be attributed to cheap and easy availability of substances in this population.

During depressive phase of their illness, 33.3% patients increased the amount of substance abuse and 20% patients decreased the amount of substance abuse in this study. Mayfield and Coleman noted that only 10% patients increased and 17% patients decreased their abusing pattern when depressed, although in most cases substance consumption did not change with affective state.[37] Some of the depressed patients increased the amount of substance abuse probably in an attempt to overcome symptoms like insomnia whereas decrease in substance abuse in other patients is seen probably due to overall lack of interest/drive in pleasurable activities. Present study shows that onset of substance abuse occurred before the onset of affective symptoms in majority (96.7%) of patients, while in just 3.3% patients, onset of substance abuse started after onset of affective symptoms. Onset of affective symptoms and onset of substance abuse occurred simultaneously in none. In a US study, Strakowski SM et al, also observed that in 70% of patients substance abuse predated bipolar illness.[25] In a population based study by Escamilla MA et al, in Costa Rica it was noted that the onset of substance abuse was before the onset of mania in 50% patients, simultaneous onset in 27% and after the onset of mania in 22% patients.[9]

Since in majority of this patients, the substance abuse had preceded the onset of bipolar disorder, the substance abuse cannot be entirely attributed to self-medication hypothesis. 27 patients in SAB group and 24 patients in NSAB group presented in their manic phase of illness. While comparing their YMRS scores, authors observed that mean total YMRS scores of SAB group of patients was greater than mean total YMRS scores of NSAB group of patients. This reflects more severe manic symptomatology in substance abusing group. In YMRS sub scores of sleep, scores were significantly more in patients of SAB group than those in patients of NSAB group ($p=0.048$) whereas insight sub scores of YMRS revealed that SAB group of patients had significantly better insight during manic phase than that of NSAB group of patients (p 0.011).

Only 3 patients in SAB group and 6 patients in NSAB group presented in depressive phase of illness. While comparing HAM-D scores of SAB and NSAB groups of patients who presented in depressed phase of illness authors did not find any significant difference in total HAM-D scores as well as in most sub-scores except in Work and activity sub score and Somatic symptoms general. SAB group of patients scored significantly more than that of NSAB group of patients on these subscales. Feinman and Dunner found that the mean scores for the depression scales were higher for the substance abusing bipolar patients.[27]

In a study by Sonne SC et al, no difference was found in average YMRS scores (5.5 vs. 4.7) and HAM-D scores (11.5 vs. 9.4) in SAB and NSAB group patients similar to this study.[21]

CONCLUSION

The salient observations of the present study were as under,

- There were no significant differences in socio demographic variables among Substance Abusing Bipolar (SAB) and Non-Substance Abusing Bipolar (NSAB) groups.
- Substance Abusing Bipolar (SAB) patients had more dysphoric and irritable mood state.
- In majority (96.66%) of Substance Abusing Bipolar (SAB) patients, the substance abuse had preceded the onset of bipolar disorder.
- Most (96.7%) of Substance Abusing Bipolar (SAB) patients during manic phase of their illness increased the amount of substance abuse.
- Manic symptomatology was more severe in substance abusing group.

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