

Co-morbidity in Bipolar Disorder: A Retrospective Study

Ravindra Neelakanthappa Munoli, Samir Kumar Praharaj, Podila Satya Venkata Narasimha Sharma

ABSTRACT

Background: Bipolar disorder is a relatively common, long-term, and disabling psychiatric illness that is associated with high levels of functional impairment, morbidity, mortality, and an increased risk of suicide. Psychiatric co-morbidity in bipolar disorder ranges from 57.3% to 74.3%, whereas medical co-morbidity varies from 2.7-70%. Indian scenario in this aspect is not clear. **Materials and Methods:** The objective was to ascertain the prevalence of physical and psychiatric co-morbidities in patients attending a tertiary care center over a period of 1 year and its relationship with socio-demographic and clinical variables. One hundred and twenty-five case record files were included in the review. OPCRIT software was used for re-establishing the diagnosis of bipolar disorder, which yielded 120 cases. A semi-structured pro-forma, specifically designed for the study, was used to collect the socio-demographic and clinical details. **Results:** Co-morbid psychiatric disorders were found in 52 (43.3%) of the sample, whereas co-morbid physical illness was present in 77 (64.2%) patients. The most common psychiatric disorder associated was substance use disorder (27.5%), whereas co-morbid cardiovascular disorder was the most frequent physical diagnosis in the sample (20%). **Discussion:** The prevalence of co-morbid psychiatric disorders in bipolar patients was lower than that reported in western literature. It could be related to retrospective nature of study or reflect true lower prevalence rates. Also, certain disorders such as eating disorders were absent in our sample, and migraine diagnosis was very infrequent.

Key words: *Bipolar disorder; co-morbidity; mood disorder*

INTRODUCTION

Co-morbidity, by definition, indicates occurrence of two syndromes in the same patient, and diagnosis of one does not categorically exclude the diagnosis of the other.^[1] Clinical co-morbidity is also mentioned as one disorder influencing a second co-existing disorder in terms of course, outcome, or treatment response.^[2] Being a relatively common, long-term, and disabling

disorder, it leads to high levels of functional impairment, morbidity, mortality, and increases risk of suicide.^[3] The co-morbidities have become a rule rather than exception, and they have increased complexity of it. The occurrence of co-morbidities has negative prognostic implications for psychological and medical well-being and longevity. Similar to models in medicine, bipolar disorder has psychiatric and medical co-morbidities, which require treatment equally as they might contribute to mood disturbance.

Lifetime psychiatric co-morbidity rates in bipolar I samples range from 50% to 70%.^[4] Lifetime prevalence for a co-morbid anxiety disorder was 51.2%, while rate for a current anxiety disorder was 30.5% in Systematic Treatment Enhancement Program for Bipolar Disorder (STEP BD); co-morbid anxiety was more common in patients with bipolar I disorder

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Department of Psychiatry, Kasturba Medical College, Manipal, Karnataka, India

Address for correspondence: Dr. Samir Kumar Praharaj,
Department of Psychiatry, Kasturba Medical College, Manipal, Karnataka - 576 104, India. E-mail: samirpsyche@yahoo.co.in

compared with bipolar II. The majority of patients with bipolar disorder I and II, of all ages and both genders, have at least one co-morbid psychiatric or medical disorder and many have more than one.^[5] In the Epidemiologic Catchment Area study, substance use disorder co-morbidity was found to exist in 61% bipolar I patients and in 48% bipolar II patients.^[6]

Co-morbid medical disorders are fairly common in bipolar patients; over 80% have at least one active medical problem, while 19-23% have 2 such conditions and 35-40% have 3 or more.^[7,8] When compared to the general population, bipolar patients have more tendency to have from cardiovascular disease, type 2 diabetes mellitus, and other endocrine disorders.^[1,9] In population-based studies, cardiovascular mortality is found to be almost twice as high in bipolar disorder patients; this may be attributed to higher rates of obesity.^[10,11]

One of the reasons for the psychiatric co-morbidity is genetic basis of these disorders. Also, the illness itself may be a precipitant factor for developing substance use and anxiety disorders. The medical co-morbidity in bipolar disorder can be result of the various factors. Most of the time, it is a blurred scenario whether a medical disorder is truly co-morbid, a consequence of treatment, or a combination of both, as this is seen in obesity, diabetes, and hypothyroidism.^[12,13]

Although the pathophysiology resulting in co-morbidity is still unknown, bipolar disorder may be a risk factor for some co-morbid Axis I diagnoses or *vice versa*. Because bipolar symptoms of mood disturbance, anxiety, and psychosis overlap with those of other psychiatric conditions, evaluating patients during remission may help differentiate among these possible mechanisms. Indian scenario in this is not quite clear, as certain diagnoses are uncommon such as eating disorders, PTSD, etc. Therefore, we aimed at studying the co-morbidity pattern in bipolar disorder and its relationship with socio-demographic and clinical variables.

MATERIALS AND METHODS

Study design and sample

This was an observational study involving retrospective file review, conducted at Department of Psychiatry, Kasturba Medical College, Manipal, a tertiary care center in Udupi district of Karnataka, India. Institutional ethical committee clearance was taken prior to the study. Sample consisted of case record files of patients admitted or evaluated in detail in the year 2010 and were diagnosed as having bipolar disorder according to ICD-10 Diagnostic Criteria for Research.^[14] The data was collected in July 2011.

Objectives

The objectives of the study was to ascertain the prevalence of physical and psychiatric co-morbidities in bipolar disorder patients who attended a tertiary care center over a period of one year, and to ascertain the relationship between socio-demographic and clinical variables and physical and psychiatric co-morbidities in bipolar disorder patients.

Tools

A semi-structured pro-forma, specifically designed for the study, was used to collect socio-demographic and clinical details of all the patients. Operational criteria checklist (OPCRIT)^[15] was used to generate lifetime diagnosis of bipolar disorder based on the details available from the file. The use of OPCRIT for psychotic and affective disorders facilitates a polydiagnostic approach to mental illness.

Procedure

All files of patients who were evaluated in detail in the year 2010 were screened for the diagnosis of bipolar disorder. Out of a total of 845 patients, 140 patients received a diagnosis of bipolar disorder. Of these, 15 files (9.33%) had insufficient data or could not be traced. The remaining 125 files were included in the study according to the inclusion criteria. OPCRIT software was used for re-establishing the diagnosis of bipolar disorder, based on the clinical data by the first author, RNM. Any ambiguity in diagnosis was resolved following a discussion with the second and third authors. One hundred and twenty patients fulfilled the diagnosis of bipolar disorder on evaluation in OPCRIT software were finally included in the study. Semi-structured pro-forma designed for the study was used to collect details of the included patients.

Statistical analysis

The collected data was statistically analyzed using Statistical Package for Social Sciences (SPSS) 16.0 for Windows. Proportions were calculated to identify the rates of co-morbidity. Association of co-morbid disorders with demographic and clinical variables was found using Pearson's chi-square test and Mann-Whitney test for categorical and continuous variables, respectively. Effect sizes were reported as phi coefficient (or Cramer's V) and point biserial correlation coefficient.

RESULTS

The sample characteristics are summarized in Tables 1a and 1b. The mean age of the patients was 39.54 (SD 15.27, range 16-80) years, and mean years of formal education was 10.55 (SD 4.72). Males were marginally greater in number than females (52.5 vs. 47.5%), and half the sample were married. Most patients

Table 1a: Sample characteristics: Demographics (N = 120)

	Mean (SD)
Age	39.54 (15.27)
Education years	10.55 (4.72)
Family size	4.19 (2.27)
	N (%)
Gender	
Male	63 (52.5)
Female	57 (47.5)
Marital status	
Single/separated	59 (49.2)
Married	61 (50.8)
Religion	
Hindu	96 (80.0)
Muslim	11 (9.8)
Christian	13 (10.2)
Occupation	
Unemployed	8 (6.7)
Employed	58 (48.3)
Student/housewife	54 (45.0)
Income (N = 116)	
Low	35 (29.2)
Middle	28 (23.3)
High	53 (44.2)
Residence	
Urban	54 (45.0)
Rural	66 (55.0)
Family type (N = 118)	
Nuclear	76 (63.3)
Joint	29 (24.2)
Living alone	13 (10.8)

were Hindus (80%) and were either employed or students/housewife. Majority were from nuclear families (63.3%). The mean age of onset was 27.07 (SD 12.69) years, and the median number of episodes was 4. Manic episodes were most frequent, followed by depressive and mixed episodes. Approximately one-third of patients had only recurrent manic episodes. Rapid cycling was present in only 4 (3.3%) patients. Family history of bipolar disorder was present in 48 (40%) patients.

Co-morbid psychiatric disorders were found in 52 (43.3%) of the sample, whereas co-morbid physical illness was present in 77 (64.2%) patients [Tables 2a and 2b]. The most common psychiatric disorder associated was substance use disorder (27.5%). Tobacco and alcohol were the most frequently used substances of abuse in this sample. Substance use was present in 29 male (87.9%) and 4 female (12.1%) patients; the difference was significant ($\chi^2 = 22.84, P < .001$, Effect size $\phi = 0.44$). Significantly higher number of patients with substance use disorder was employed ($\chi^2 = 25.04, P < .001$, Effect size Cramer's $V = 0.46$). A higher trend towards substance use disorder was found in Hindu patients, as compared to other groups ($\chi^2 = 5.09, P = .078$, Effect size Cramer's $V = 0.21$).

Table 1b: Sample characteristics: Clinical (N = 120)

	Mean (SD)
Age of onset of illness	27.07 (12.69)
Total number of episodes (N = 116)	7.45 (8.94)
Median (IQR)	4 (7)
Number of manic episodes (N = 116)	4.91 (6.28)
Median (IQR)	2 (5)
Number of depressive episodes (N = 116)	2.16 (3.78)
Median (IQR)	1 (2)
Number of mixed episodes (N = 116)	0.37 (0.81)
Median (Range)	0 (4)
Duration of illness in years	12.53 (11.86)
Age at first hospitalization	27.42 (12.81)
Number of suicide attempts (N = 11)	1.36 (0.67)
Median (Range)	1 (2)
	N (%)
Family psychiatric illness	
Present	96 (80.0)
Family mood disorder (N = 67)	
Bipolar disorder	48 (40.0)
Depression	5 (4.2)
Family physical illness (N = 119)	
Present	41 (34.2)
Bipolar type	
BAD I	76 (63.3)
BAD II	5 (4.2)
Recurrent mania	38 (31.7)
Rapid cycling	
Present	4 (3.3)
Past suicide attempt	
Present	10 (8.3)
Co-morbid psychiatric illness	
Present	52 (43.3)
Co-morbid physical illness	
Present	77 (64.2)

Nineteen (57.6%) with bipolar I subtype had substance use disorder, which was significantly higher than other groups ($\chi^2 = 7.14, P = .028$, Effect size Cramer's $V = 0.25$). There was significantly earlier age of onset (Mann-Whitney $U = 897, Z = -3.17, P = .002, r_{pb} = 0.27$) and age at first hospitalization (Mann-Whitney $U = 880, Z = -3.27, P = .001, r_{pb} = 0.29$) in patients with substance use disorder.

Co-morbid anxiety disorder was present in 13 (10.8%) patients, and anxiety disorder unspecified was the most common diagnosis (4.2%) followed by generalized anxiety disorder (2.5%). There was no significant association of anxiety disorder co-morbidity with demographic and clinical variables.

Co-morbid cardiovascular disorder was the most frequent physical diagnosis in the sample (20%). Significantly higher rates of co-morbid cardiovascular disorder were associated with higher age (Mann-Whitney $U = 414, Z = -4.84, P < .001, r_{pb} = 0.47$), age of onset of illness (Mann-Whitney $U = 558, Z = -3.90, P < .001, r_{pb} =$

Table 2a: Co-morbid psychiatric disorder (N = 120)

	N (%)
Substance abuse	33 (27.5)
Substance abuse subtype	
Tobacco only	12 (10)
Alcohol only	5 (4.2)
Alcohol and tobacco	12 (10)
Others	4 (3.3)
Anxiety disorder	13 (10.8)
Anxiety disorder subtype	
GAD	3 (2.5)
OCD	2 (1.7)
Panic disorder	1 (0.8)
Social phobia	1 (0.8)
PTSD	1 (0.8)
Unspecified	5 (4.2)
Personality disorder	5 (4.2)
Mental retardation	5 (4.2)
ADHD	3 (2.5)
Dementia	2 (1.7)
Mild cognitive impairment	1 (0.8)

Table 2b: Co-morbid physical disorder (N = 120)

	N (%)
Cardiovascular disorder	24 (20.0)
Cardiovascular disorder subtype	
Hypertension	21 (17.5)
Coronary artery disease	1 (0.8)
Congestive cardiac failure	1 (0.8)
Peripheral vascular disease	1 (0.8)
Hypothyroidism	19 (15.8)
Diabetes mellitus	13 (10.8)
Dyslipidemia	12 (10.0)
Obesity	12 (10.0)
Skin disorders	12 (10.0)
Anemia	10 (8.3)
Osteoarthritis	5 (4.2)
Epilepsy	3 (2.5)
Asthma	3 (2.5)
Migraine	2 (1.7)
HIV infection	1 (0.8)
Hyperthyroidism	1 (0.8)

0.44), and age of first hospitalization (Mann-Whitney $U = 577$, $Z = -3.78$, $P < .001$, $r_{pb} = 0.43$). A trend towards longer duration of illness was associated with presence of co-morbid cardiovascular disorder (Mann-Whitney $U = 855$, $Z = -1.95$, $P = .051$, $r_{pb} = 0.14$). Hypothyroidism was found in 19 (15.8%) patients; it did not show any association with demographic and clinical variables.

DISCUSSION

In our study, we found out the prevalence of at least one psychiatric co-morbidity with bipolar disorder to be 43%, which was lower than that of previous studies

where it ranged from 57.3% to 74.3%.^[16,17] Co-morbid physical illness in our sample of bipolar patients was 64.2%; in previous studies, it varied from 2.7% to 70%, which has been attributed to differences in study designs and differences in sample.^[7]

In our study, the prevalence of substance use disorder was 27%, which was the most common psychiatric co-morbidity. Compared to previous studies, in which co-morbid substance use disorders in bipolar disorder ranged from 34% to 60%, the rates are lower in our study.^[1] The rate of tobacco use was 20%, which was lower than 51% to 70% reported across various studies.^[18,19] Similarly, alcohol use was only 14.2% as compared to previous reported rates of 30% to 69%.^[1] It is interesting to note that reports from Taiwan suggest lower lifetime rate of substance abuse in bipolar patients (10%).^[20] Thus, the higher rates might be primarily restricted to Western societies. The lower prevalence of substance use in our sample could reflect the general lower rates in females as it is culturally less acceptable in our society. The male predominance of substance use in our sample had strong effect size. The onset of bipolar illness was earlier in those having substance use co-morbidity, and the age of first hospitalization was lower, suggesting a severe form of illness in these patients. The effect sizes for these associations were small. Current study findings are similar to the study by Winokur *et al.* in which bipolar patients with alcoholism had a significantly younger age of onset (mean of 23 years) than those without (mean of 27 years).^[21]

In STEP-BD, the lifetime prevalence of co-morbid anxiety disorder was 51.2%; prevalence of co-morbid panic disorder varied from 3%-21%, for OCD 2%-21%, for PTSD 39%, for social phobia 22%.^[5] In our sample, the prevalence of anxiety disorder was much lower (10.8%). Similarly, higher prevalence of co-morbid personality disorders has been reported, which varies from 28% to 40% across studies.^[1] In our study sample, the prevalence of personality disorder was only 4.2%, which might be an underestimate due to lack of use of structured instruments in routine clinical practice. Outcome in bipolar illness is worse in the presence of a co-morbid anxiety disorder and poses difficult challenge in the treatment since anti-depressants may alter the course of bipolar disorder.^[22]

In our study, co-morbid cardiovascular disorders were the most common physical diagnosis and were found in 20%, and hypertension accounted for 17.5% of these patients. Previous studies reported much higher lifetime prevalence rates of cardiovascular disorders in bipolar patients (up to 48%).^[7] The lifetime co-morbid prevalence for hypertension is found in 34%,^[8] twice

that of our study. There were increased rates of co-morbid cardiovascular disorders with higher age and later age of onset of illness, and the effect sizes were medium. Such association has been found in previous studies too.^[23,24]

Prevalence of co-morbid hypothyroidism in lithium-naïve patients was found in 9%, and the rates of overt hypothyroidism vary from 0% to 47% (average of about 10%) among patients on long-term treatment with lithium.^[25,26] In our study, the prevalence of co-morbid hypothyroidism was 15.8%, similar to the previous studies. Overt hyperthyroidism is uncommon in bipolar disorder; its prevalence is no greater than 2% across different studies.^[26] In our sample, prevalence of hyperthyroidism was 0.78%.

Interestingly, several co-morbid conditions in bipolar disorder have been reported in western literature, but were absent or less prevalent in our sample. For example, higher rates of eating disorder have been reported in bipolar disorder,^[27] though we did not find a single patient with such diagnosis. Migraine was present in only 2 (1.7%) patients in our study sample, whereas prevalence of co-morbid migraine varies from 15%-40% across studies.^[11]

A major limitation of our study includes retrospective design, which has inherent bias and might have contributed to the underdiagnosis of co-morbid disorders in our sample. It might as well reflect true lower prevalence of co-morbid disorders in our country as compared to western studies. One possible explanation could be the higher threshold for diagnosis of certain disorders (e.g. personality disorder) in our country. Another limitation was medication details have not been addressed, which might have contributed to the differential prevalence of physical co-morbidities, specifically, cardiovascular co-morbidities. The use of OPCRIT criteria to confirm diagnosis of bipolar disorder was strength in our study. Further studies with prospective design could provide greater insight in to the true prevalence of co-morbid disorders.

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