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Original Research Article

Clinical Correlates of Metabolic Parameters inBipolar Disorder: A Cross Sectional Study

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Abstract

Background: People with bipolar disorder develop a host of physical problems which affect its course and outcome in an unfavorable manner. Many of the physical symptoms observed in bipolar disorder are components of the metabolic syndrome. Metabolic derangements like obesity, abnormal glucose levels, abnormal lipid profile, and thyroid dysfunction, are highly prevalent in these patients due to shared etiological factors.

Methods: A cross-sectional study was conducted in the psychiatry department of PMCH Patna. for a period of about one an half year. All patients fulfilling the ICD-10 criteria for bipolar disorder attending the clinical services of the department of psychiatry were included in the study. A total of 67 consenting patient were assessed by using a pretested structured proforma, life chart was drawn to assess course of illness, the severity of present episode was assessed by Young Mania rating Scale (YMRS) for mania and Hamilton Depression Rating Scale (HAMD) for depression.

Conclusion: This study aimed to explore the relationship of metabolic syndrome and bipolar disorder. The prevalence of metabolic syndrome found to be 53.7%. Patients with metabolic syndrome were found to have greater numbers of lifetime depressive episodes. Considering the high prevalence ofmetabolic syndrome in the patients of bipolar disorder; strategies have to be developed for prevention, early detection and treatment of the same.

Keyword: Bipolar Disorder, Metabolic Syndrome.

Introduction

Bipolar disorder (BD) is a chronic, episodic illness with frequent exacerbation of mania and depression. Episodes are usually separated by periods of recovery, with return to normal function. Jules Falert provided one of the earliest historical accounts of bipolar disorder and called it as “la folie circulare” Later the concept was further redefined when Emil Kreplin segregated it from other psychotic illnesses leading to the separation of “Manic Depressive Psychosis” from “Dementia Precox.” However, the course of bipolar disorder is not entirely beningn, with recent research is suggesting that patients with bipolar disorder experience significant degree of chronicity than previously thought. Epidemiological studies indicate increased rate of mortality among BD patients as compared to the general

population. One of the major factors conditioning to this is the occurrence of obesity, hypertension, dyslipidaemia, abnormal glucose levels among these patients. Metabolic syndrome, which is a constellation of metabolic abnormalities, tends to share common risk factors with bipolar disorder. It is now identified as the risk factor for cardiovascular disease and diabetes type-2. These findings emphasize the need for identification and early intervention of metabolic abnormalities which can modulate the severity of the illness to a great extent and reduce the morbidity & mortality associated with the illness. Most of the present data on metabolic syndrome in BD emanates from western studies. India is reported to have higher rate of early onset diabetes and hypertension. With this background thereis a need to explore the relationship between metabolic abnormalities and bipolar disorder in Indian context. Our study is one of such attempt.

Objectives

To assess the extent of various metabolic parameters (including anthropometric ie; body weight, height, basal metabolic index, and biochemical like blood glucose level, thyroid profile, lipid profile, and liver functions test) in patients with bipolar disorder.

To examine relationship between these metabolic abnormalities and the severity of bipolardisorder.

To explores the relationship between clinical variables of importance in bipolar patients andmetabolic parameters.

Material and Method

Cross Sectional type, sampling done by purposive sampling. The present study was conducted at psychiatry department of Patna medical College and Hospital Patna, Bihar. Study duration One and half years. Total 67 patients of bipolar disorder have been included in the study.

Inclusion criteria

- Patients diagnosed with bipolar disorder according to International Classification ofDisease, Tenth edition -WHO (ICD-10).
- Age18 to 50 years.
- Those patients who consent to be a part of the study

Exclusion criteria

- Patients who are in an altered sensorium.
- Past history of (prior to the current illness and initiation of medication); diabetes mellitus, hypertension, ischemic heart disease, thyroid dysfunction, and treatment of these disorders.
- Pregnancy and postpartum (< 6 weeks after delivery or miscarriage).

The study was carried out at the Department ofPsychiatry of PMCH Patna. Adult (aged more than 18 years) male and female patients diagnosed with bipolar disorder according to ICD-10, were invited to participate in the study, a written informed consent was obtained from all the patients prior to recruitment in to the study. Socio-demographic characteristics and clinical details of all the subjects were recorded in astructured proforma developed by the department of psychiatry for the study.

Sample was selected by purposive sampling and allocated to the inclusion or exclusion group.

70 patients diagnosed with bipolar disorder were approached over a periode of 19 months. 2 patients declined participation and 1 patient was excluded because of higher age (patients morethan 50 years are excluded). A detailed assessment of anthropometric parameters like height (cm), body weight (kg) and body mass index (BMI), waist circumference measured (cm) was made. Fasting venous blood sample was collected with aseptic precautions and sent to laboratory for the examination for blood glucose, serum lipid, and thyroid profile.

The severity of symptoms of present depressive episode was assessed by using HamiltonDepression Rating Scale (HDRS). The severity of present manic episode was assessed by using Young Mania Rating Scale(YMRS). Metabolic syndrome (MetS) was ascertained by using a consensus definition[56] according to which three or more criteria are required to be satisfied. The criteria are high blood pressure (≥130/85), high triglycerides level (>150 mg/dl), low level of HDL (<40 mg/dl for male and <50 mg/dl for female), impaired fasting sugar (≥100 mg/dl), and high waist circumference (>90cm for males and >80 cm for females) The Young Mania Rating Scale (YMRS) is one of the most frequently utilized rating scales to assess manic symptoms. The scale has 11 items and is based on the patient's subjective report of his or her clinical condition over the previous 48 hours. Additional information is based upon clinical observations made during the course of the clinical interview. The items are selected basedupon published descriptions of the core symptoms of mania. The YMRS follows the style of the Hamilton Rating Scale for Depression (HAM-D) with each item given a severity rating. There are four items that are graded on a 0 to 8 scale (irritability, speech, thought content, and disruptive/aggressive behavior), while the remaining seven items are graded on a 0 to 4 scale. These four items are given twice the weight of the others to compensate for poor cooperation from severely ill patients. There are well described anchor points for each grade of severity. The authorsencourage the use of whole or half point ratings once experience with the scale is acquired. Typical YMRS baseline score scan vary a lot. They depend on the patients' clinical features such as mania (YMRS = 12), depression (YMRS = 3), or euthymia (YMRS = 2). Sometimes a clinicalstudy entry requirement of YMRS > 20 generates a mean YMRS baseline of about 30. Strengths of the YMRS include its brevity, widely accepted use, and ease of administration. The usefulnessof the scale is limited in populations with diagnoses other than mania.

Results

A total of 67 patients were studied. Results are describes under the following headings:

- Socio-demographic variables.
- Illness variables.
- Anthropometric and Metabolic Parameters.
- Prevalence of MetS and its component.
- Clinical correlation of MetS in bipolar disorder.

Socio-demographic details: The mean age of the sample was 37.32 years with 44 male and 23 female. Majority of patients were from urban locality (82.1%) and Hindu by religion (89.6%). 55.2% patients were on payment job, with women being mainly housewives, at the time of assessment. The mean duration of the illness was 12.95 years. The mean age was greater for the patient with metabolic syndrome (MetS) than those without MetS (40.8 Vs 33.3).

Illness variables

The mean age of onset of bipolar disorder was 24.37 years. Majority had mania as first episode (N=46 ; 68.7%) with the mean age of 25.9 years followed by Depressive episode (N=17; 25.4%) with mean age of onset 23.6 years, mixed episode (N=4 ; 6%) with mean age of 21.37.

Table 1

Nature of the episode	Mean age of onset (±SD) Yrs
Mania	25.91±8.1
Depression	23.64±81
Mixed	21.37±8
Hypomania	No patients reported

Following table describe numbers of lifetime episodes. On an average patient had 2.6 manic,

1.5depressive, and 0.34 mixed episodes.

Table 2

	Mean Numbers (±SD)
Numbers of lifetime manic episodes	2.657±2.52
Numbers of lifetime depressive episodes	1.50±1.87
Numbers of lifetime mixed episodes	0.34±0.789
Total lifetime episodes.	4.49±3.006

Following table enumerates the nature of current episode. Majority were having a manic episode(43.6%), While 23.5% were in depression, hypomanic features were present in 7.4% while 3% were in a mixed episode. 22.1% patients were in remission.

Table 3

Nature of the current episode	**No. of patients (%)**
Mania	29(43.6%)
Depression	16 (23.5%)
Hypomania	5 (7.4%)
Mixed	2(3%)
Remission	15(22.1%)

Details of the substance use in the sample.

Table-4

Substance	**N (%)**	**Use N (%)**	**Abuse N(%)**	**Dependence N(%)**
Alcohol	29 (43.28%)	10 (14.9%)	8(11.9%)	11(16.4%)
Nicotine	26(38.80%)	7(10.4%)	6(9%)	13(19.4%)

Following table shows the distribution of patients of bipolar disorder with Mets with Alcohol use.

Table 5

Alcohol Use				
		MetS		**Total**
		YES	**NO**	
Alcohol Use	YES	18	12	30
	NO	18	19	37
Total		36	31	67

Following table enumerates the use, abuse and dependence of Alcohol and Nicotine in the patients withMetS and without MetS.

Table 6

Substance		**MetS+BD**	**BD**
		N=18	**N=11**
Alcohol (N=29)	Use	7	3
	Abuse	4	4
	Dependent	7	4
Nicotine (N=26)		N=15	N=11
	Use	5	2
	Abuse	3	3
	Dependent	7	6

Following table shows the result of Simple binary logistic regression analysis. The

factors included are age of patients, numbers of lifetime episodes, numbers of life time mania, numbers of lifetime depressive episodes, duration of untreated illness, dose and duration of Valproate, Olanzapine, lithium and quitipine. Finally age of the patients, numbers of lifetime depressive episodes and Olanzapine use was found to be predictive.

Table 7

	B	SE	Wald	Significant	CI
Age	0.099	0.039	6.361	0.012	0.839-0.978
Number of Depressive episodes	0.893	0.319	7.819	0.005	0.219-0.766
Olanzapine dose	0.420	0.189	4.929	0.026	1.050-2.205

P<0.05 considered as significant; age, numbers of life time depressive episodes and Olanzapine dosage found to have predictive value.

Discussion

In the present study we examined 67 patients with the diagnosis of bipolar disorder who attended department of psychiatry of PMCH Patna hospital. We conducted a thorough physical examination and clinical assessment. Patients were assessed for the metabolic abnormalities like obesity, hypertension, diabetes, dyslipidemia, and thyroid functions. Our aim was to assess the extent to which these metabolic abnormalities are present in the given sample anddelineate as to how many of them qualify for a diagnosis of metabolic syndrome. In additionwe wanted to discern the relationship between metabolic syndrome and the severity of the present state as well as course variables of bipolar disorder. Studies from west have concluded that the metabolic syndrome and its components are interwoven with the disease progression and appear to be powerful determinants of the course of bipolar disorder. [1,2] The linkages between metabolic syndrome and bipolar disorder have not been explored in Indian context despite growing rates of early onset of diabetes and hypertension. In the present study in addition to examining the prevalence of MetS in bipolar patients an effort has been made to explore its relationship with the type of index episode, total numbers of life time episodes, and severity of the current episode. This particular aspect hasn't received attention in the Indian context. The patients of BD with MetS were found to be much older than patients with MetS alone. [3,4,5,6] A review of 34 studies across the world shows prevalence ranging from 16.7 to 67% with a mean age ranging from 34.1 to 55.7 years. A recent meta-analytic investigation [7] (33 studies, N=6,286) revealed that the prevalence of MetS across studies was37.3% with a mean age of 42.8 years. Study by Grover et al, which was the first of its kind regarding this aspect in Indian context, reported a prevalence of 41% MetS in patients of bipolar disorder with mean age of 39 years. In our study mean age of patients of BD with MetS is 40.8±8.4 years as compared to these bipolar patients without MetS (33.29±9.4 years) and the prevalence was 53.7%. These findings are consistent with the existing literature.

Gender and metabolic syndrome in bipolar disorder: Studies which analyzed the age adjusted prevalence [8,9] of MetS with regard to gender in BD give variable findings. The prevalence of MetS was less in European women as compared to men (14.4%Vs 18.4%), while South Asian men were having lesser rate of MetS as compared to women (28.8%Vs 31.8%). And studies conducted in United States also show a higher prevalence of Mets in women (23.7% Vs 15.7%). Grover et al in his study reported that 61 men and 21 women satisfied the modified NCEP ATP-III criteria, [10] which thus showed the prevalence of MetS was higher in men (43.57% Vs 35%). In our study 25 men and

11 women met the criteria (69.44% Vs 30.55%) for MetS showing a higher prevalence ofmetabolic syndrome in men than in women which in tune with the above Indian study. The waist circumference (WC) is the measurement of abdominal fat and an easily measurable component of metabolic syndrome. High WC is seen commonly in bipolar patients as compared to age matched control group. In their review Grover et al report that the prevalence of waist circumference ranges 30% to 61% among BD patients. There was a higher prevalence in the present study (73.5%) with WC being more among men compared towomen. While BMI offers the best estimate of total body fatness, WC gives an estimate of visceral fat and risk of obesity related diseases. Patients with bipolar disorder have a high prevalence of hypertension and increased risk of mortality due to cardiovascular disease. [11,12,13] In their review Grover et al report that the prevalence of hypertension in patients of bipolar disorder ranges from 18.6% to 78.1%. In thepresent study 35.3% patients were hypertensive which is within the range reported in the literature. However the role of antihypertensive medications in modulating the prevalence hasto be taken into consideration. Studies across the world show a high prevalence of dyslipidemia in patients of bipolar disorder. [14] In a recent review of 34 studies Grover et al report that the prevalence of low HDL level across the 19 studies was ranging from 21.7% to 67.6% and high triglyceride range from 22.7% to 58.8%. In the present study 70.6% of patients were having low HDL level while 63.2% were having high triglyceride level. These findings are again consistent with the previous studies. Impaired glucose tolerances and insulin resistance is found to be more common in individualswith bipolar disorder than in the general population. [15] Grover et al reported that the prevalence of high FBS across 19 studies ranges from 6% to 32.4%. In the present study 32.4% patients were having high FBS which is in tune with the findings in the literature. Multiple factors affect the occurrence of metabolic syndrome in bipolar patients. Western studies suggest that longer duration illness [16,17] and age more than 35 years can be a strong predictor for the development of MetS, which has been replicated by Grover et al [18] in the Indian context. A binary logistic regression analysis was carried out to identify predictors of MetS in the present study. Age, number of lifetime depressive episodes and use of olanazapine emerged as significant predictors [19]

Conclusion

The present study is a cross sectional study done on 67 patients with a diagnosis of Bipolar Affective Disorder with a view to examine the presence of Metabolic Syndrome and its clinical correlates. The study was conducted in a general hospital psychiatric unit. A detailed clinical history was taken using a life chart. Anthropometric measurements were taken, relevant biochemical investigations to assess metabolic changes were done and the severity of thecurrent clinical episode was assessed using relevant scales. The mean age of the study population was 37 years. Two thirds of them were males, majority of them being from urban areas, educated up to secondary level. Half the population was employed, with women being mainly housewives. Majority were Hindus.

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