# Prevalence of metabolic syndrome and its clinical correlates among patients with bipolar disorder

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ABSTRACT

Objective: To assess the prevalence of metabolic syndrome (MetS) in patients with bipolar disorder (BD) and examine the clinical correlates of MetS.
Methods: Sixty-seven patients with BD were evaluated for presence for MetS. The consensus definition was used to define MetS. The clinical variables were recorded on the basis of information provided by the patients, accompanying caregivers and review of treatment records. The symptoms severity of present depressive and manic episode was assessed by using Hamilton Depression Rating Scale (HDRS) and Young Mania Rating Scale (YMRS) respectively.
Results: The prevalence of MetS was 53.7%. Patients with MetS were older than the patients with BD alone (P = 0.001). Increased waist circumference was the most common abnormal parameter (74.6%) followed by low high density lipoprotein (HDL) (71.6%) and raised triglycerides (64.2%). High blood pressures were recorded in 35.8% with high fasting blood glucose levels were seen in 33.3%. MetS was associated with greater number of life time episodes (p = 0.010), longer duration of illness (p = 0.010), greater numbers of lifetime depressive episodes (p < 0.001). Substance use (alcohol and nicotine) associated with significantly higher prevalence of high blood pressure among MetS patients (p < 0.001) while abnormal triglyceride level shown associated with substance use (p = 0.010). Age of the patients, number of lifetime depressive episodes and use of Olanzapine were found to predictive of the development of MetS.
Conclusions: Patients with BD have high prevalence of MetS and its presence correlates with clinical variables.

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## 1. Introduction

Metabolic syndrome (MetS), a constellation of metabolic abnormalities, tends to share common risk factors with bipolar disorder (BD) (Elmslie et al., 2001; Ford et al., 2005; Lakka and Bouchard, 2005). Epidemiological studies indicate an increased rate of cardiovascular mortality among patients with BD compared to the general population (Angst et al., 2002; Fagiolini et al., 2005, 2003; Klumpers et al., 2004; Osby et al., 2001). Lifestyle and behavioural patterns might play an important role in the occurrence of the MetS in patients with BD like lack of exercise

(Fagiolini et al., 2003; Ford et al., 2004; Malhotra, 2003) poor eating habits (Elmslie et al., 2001) and especially substance use are the important contributors (Brady and Lydiard, 1992; Grant et al., 2004a,b). Many studies across the world have reported the prevalence rate of MetS in patients with BD to be 16.7% to 67% (Grover et al., 2012b) However, there is limited data on the clinical correlates of MetS in patients with BD. Existing data suggests that presence of MetS among patients with BD is associated with clinical variables like longer duration of illness (Chang et al., 2009; Salvi et al., 2008), more occurrence of bipolar disorder-I subtype (Chang et al., 2009), higher number of lifetime depressive and manic episodes, first episode and current episode being depression (Fagiolini et al., 2008), more severe and difficult-to-treat index affective episode (Fagiolini et al., 2005) lower severity of mania during the index episode (Garcia-Portilla et al., 2008) later age of onset at first manic episode, later age at first treatment (McIntyre et al., 2010) less healthy diet as rated by patients themselves, absence of physical activity and family history of diabetes mellitus

(Van Winkel et al., 2008) Some of the studies also suggest association of MetS among patients with BD with substance abuse. The National Epidemiologic Survey on Alcohol and Related Condition (NESARC) assessed the co-morbidity of nicotine and substance abuse disorder with mood and anxiety disorders, in a nationally representative sample of 43093 respondents, and found that 35.3% of individuals with a history of hypomania met the criteria for nicotine dependence compared with 12.8% of the general population (Grant et al., 2004a,b). The NESARC study estimated the 12-month prevalence of substance use disorders to be 27.9% and 26.6% among individuals with a history of mania and hypomania respectively, as compared to 9.4% in the general population (Grant et al., 2004a,b). In an another observation (Chengappa et al., 2000) 70% of outpatients of bipolar disorder were nicotine dependent and even the alcohol use and abuse was on higher than seen in general population. Specifically, rates of alcohol use among patients with bipolar disorder have been reported in the range of 21.4–54.5% (Pini et al., 2005).

Most of the present data on MetS in patients with BD emanates from western studies with occasional studies from India (Grover et al., 2014a,b, 2012a,b). However, the studies from India have not evaluated the clinical variables in details, and there is lack of data in terms of association of MetS among patients with BD with clinical variables and substance use in the Indian setting. With this background, this study attempted to explore the prevalence and clinical correlates of MetS among patients with BD.

## 2. Material and method

The study was carried out at the Department of Psychiatry of Kempegowda Institute of Medical Sciences (KIMS) in Bangalore, India. The study protocol was presented to the Ethical Review committee of Kempegowda Institute of Medical Sciences (KIMS) and was duly approved. The study was carried out in accordance with the Declaration of Helsinki. Adult (aged 18–50 years) patients diagnosed with BD according to ICD-10 (World Health Organisation, 2012) after written informed consent were included in the study. Patient in altered sensorium, with past history (prior to the current illness and initiation of medication) of diabetes mellitus, hypertension, ischemic heart disease, thyroid dysfunction, and women during pregnancy and postpartum (<6weeks after delivery or miscarriage) were excluded from study. Socio-demographic characteristics and clinical details of all the subjects were recorded in a structured Performa. Seventy patients with the diagnosis of BD were selected by purposive sampling over a period of 19 months (November 2011 to June 2013); two patients declined participation and one patient was excluded because of higher age (patients aged >50years). Hence, final study sample comprised of 67 patients.

### 2.1. Assessment

Body weight was measured in kilograms (kg) and height was measured in centimeters (cm) using a calibrated scale. Body mass index (BMI) was calculated from the above information. Waist circumference was measured cm, at a point midway between the inferior costal margin and the superior iliac crest, at the end of normal expiration while standing. Standard mercury manometer was used to measure blood pressure (BP) in supine position. Two readings at 5-min intervals were taken and if high blood pressure ($\geq$130/85) was noted in one of the readings, then a third reading was taken after 30 min; the lowest of these readings was included for analysis. Fasting venous blood sample was collected with aseptic precautions and send to laboratory for the examination for blood glucose and serum lipids. MetS was ascertained by using a consensus definition (Alberti et al., 2009) which was proposed in a joint interim statement of the International Diabetic Federation

Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity which provide a differential profile for Asian population (abdominal circumference of $\geq$90 and $\geq$80 cm respectively for men and women of Asian origin) according to which $\geq$3 criteria are required to diagnose MetS. The criteria are high blood pressure ($\geq$130/85), high triglycerides level (>150 mg/dl), low level of High Density Lipoprotein (HDL) (<40 mg/dl for male and <50 mg/dl for female), impaired fasting glucose ($\geq$100 mg/dl), and high waist circumference (WC) (>90 cm for males and >80 cm for females). The individuals detected with metabolic abnormalities were informed and educated about the need for proper diet and exercise and were referred to appropriate medical specialty clinics for further care.

The clinical variables were recorded on the basis of information provided by the patients, accompanying caregivers and review of treatment records. Similarly the conclusion about use of various substances was based on the above sources of information. The severity of symptoms of present depressive episode was assessed by using Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960) and the severity of present manic episode was assessed by using Young Mania Rating Scale (YMRS) (Young et al., 1978).

The Statistical Package for Social Science (SPSS) version 16.0 was used for statistical analysis. Mean and standard deviation (SD) were calculated for continuous variables. Frequencies with percentage were calculated for nominal and ordinal variables. Chi-square and $t$-test/ANOVA were used for comparisons as applicable. Pearson's correlation test was employed to examine the relationship between MetS and clinical variables. Mann Whitney test was applied if standard deviation more than mean. A p value of $\leq$0.05 was considered to be statistically significant. Binary logistic regression was performed to examine the influence of independent variables on presence of MetS.

## 3. Results

Out of the 67 patients included in the study, 36 (53.7%) of patients fulfilled the criteria for MetS according to consensus definition (Alberti et al., 2009). The mean age of the sample was 37.32 years with majority of the patients being male (N = 44; 65.7%). Majority of the patients were Hindus (89.6%), were residing in urban locality (82.1%) and 59.7% of patients were educated up to secondary or higher levels. More than half (55.2%) were on paid job. When the sociodemographic profile of those with and without MetS was compared (see Table 1) patient with MetS were older than the patient without MetS (40.8 $\pm$ 8.4 Vs 33.29 $\pm$ 9.4; P = 0.001). Clinical details of the patients are shown in table-1. The average age of onset of BD was 24.37 years. The mean duration of the illness was 12.95 years. In terms of current episode, 50.74% were experiencing a manic episode at the time of assessment; while 25.37% were in depression and about one-fourth (23.88%) were in remission. When those with and without MetS were compared it was seen that those with MetS had significantly longer illness duration (15.36 $\pm$ 7.9 Vs 10.16 $\pm$ 8.12 yrs; p = 0.010), higher number of lifetime depressive episodes (2.1 $\pm$ 2.2 Vs 0.77 $\pm$ 0.88;− p < 0.001- Mann Whitney $U$ test value 272) and higher number of total life time episodes (5.08 $\pm$ 3 Vs 3.8 $\pm$ 2.9; Mann Whitney $U$ test value 357; p = 0.010).

In addition the current level of symptoms as assessed by the relevant scales showed that those with MetS have more depressive symptoms (8.9 $\pm$ 9 Vs 5.7 $\pm$ 8; p = 0.173) and less manic symptoms (10.9 $\pm$ 11.9 Vs 17.9 $\pm$ 12.6; p = 0.023). The lag period to treatment among BD patients with Mets was found to be comparable (82.9 $\pm$ 221 Vs 63.9 $\pm$ 260 months; p = 0.882); In terms of medications used, there was no significant difference in the dose and