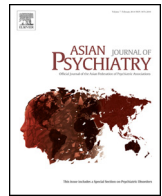




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Cardiovascular risk factors among bipolar disorder patients admitted to an inpatient unit of a tertiary care hospital in India

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ABSTRACT

Objective: The study aimed to examine the prevalence of cardiovascular risk factors in patients with bipolar disorder.

Methods: By consecutive sampling, 93 inpatients (aged ≥ 20 years) diagnosed with bipolar disorder were evaluated for 10 year coronary heart disease (CHD) risk and 10-year cardiovascular mortality risk (CMR) on the Framingham (10-year all CHD events) function/risk equation and Systematic Coronary Risk Evaluation (SCORE) respectively.

Results: Ten-year CHD risk was 3.36% and 10-year CMR was estimated to be 1.73%. One tenth (10.7%) of the sample was found to have very high/high CHD risk (≥ 10) and 6.45% of the sample had high CMR risk (≥ 5). More than half (54.88%) of patients had metabolic syndrome. Compared to females, males had higher Framingham function score (4.09 ± 5.75 vs 1.59 ± 1.05 , U value = 634.5*, $p < 0.05$) and had higher very high/high CHD risk (≥ 10) (15.1% vs 0, χ^2 4.58, $p < 0.05$).

Conclusions: Findings of the present study suggest the presence of cardiovascular risk factors and higher rate of metabolic syndrome in patients with bipolar disorder. Considering this fact, there is an urgent need for routine screening for cardiovascular risk factors in these patients. Mental health professionals should be aware of these risks; there is need to develop preventive strategies to reduce the cardiovascular risk in this population.

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1. Introduction

Cardiovascular disease is one of the leading causes of mortality in patients with severe mental illness including bipolar disorder (Osby et al., 2001; Colton et al., 2006). Although a number of studies have evaluated the prevalence of metabolic syndrome in patients of bipolar disorder (Basu et al., 2004; Fagiolini et al., 2005; D'Mello et al., 2007; Teixeira and Rocha, 2007; Yumru et al., 2007; Correll et al., 2008; Fiedorowicz et al., 2008; Garcia-Portilla et al., 2008; Salvi et al., 2008; Sicras et al., 2008; Van Winkel et al., 2008; Elmslie et al., 2009; John et al., 2009; Vuksan-Cusa et al., 2009; Chang et al., 2010; Guerreiro et al., 2010; Kemp et al., 2010; Maina et al., 2010), very few studies have assessed the prevalence of cardiovascular risk factors in patients with bipolar disorder (Correll et al., 2008; Garcia-Portilla et al., 2009). The cardiovascular

risk in these studies has been calculated as the Framingham risk equation, which provides a validated calculation of 10-year risk of development of coronary heart disease (CHD) (Wilson et al., 1998; D'Agostino et al., 2000) and the Systematic Coronary Risk Evaluation (SCORE) function indicating 10 year cardiovascular mortality risk (CMR) (Conroy et al., 2003), both of which predict 10 year risk of having a cardiovascular event. Basically, the cardiovascular risk factors included for these evaluations have considerable overlap with the parameters used for defining metabolic syndrome and additionally use smoking status and age of the subject to estimate the cardiovascular risk. Recognition of these factors is emphasized as most of these are modifiable risk factors which, if identified and managed properly, in time can contribute to reduction in cardiovascular mortality. Correll et al. (2008) reported a 10-year CHD risk of 4.7% for inpatients with bipolar disorder ($N = 74$) and 19% of their patients had high/very high risk of CHD (≥ 10). Another study reported 10-year CMR to be 1.8% and the 10 year CHD risk to be 7.6% in patients with bipolar disorder. Both these variables had significantly higher prevalence in males compared to females (Garcia-Portilla et al., 2009).

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Although a few studies have evaluated the prevalence of metabolic syndrome (MS) in patients with bipolar disorder from India (Grover et al., 2012a,b, 2014), none of the studies from India have evaluated the prevalence of cardiovascular risk factors in patients with bipolar disorder. In this background the current study aimed at estimating cardiovascular risk as the Framingham function/risk equation for development of CHD, the SCORE function – 10 year CMR, in patients with bipolar disorder.

2. Method

The study was approved by the Ethics Review Committee of the Institute. The study was carried out at the inpatient unit of a multi-specialty tertiary-care hospital in North India. Consecutive patients (aged 20 or above), admitted to the inpatient unit from January 2009 to December 2011 with bipolar disorder according to the International Classification of Diseases – Classification of Mental and Behavioral Disorders – Clinical Descriptions and Diagnostic Guidelines tenth revision (ICD-10) (World Health Organization, 1992) were included. Informed consent was sought from all patients who were part of this study. If the patient was incompetent on account of illness to provide informed consent, the primary caregiver staying with the patient was approached to provide informed consent. Patients were recruited during the first week of their admission to the inpatient unit.

Assessments of the patients involved evaluation for cardiovascular risk factors and MS profile. Data with respect to the prevalence of MS for a subgroup of this cohort was published earlier (Grover et al., 2014).

Framingham risk equation (Wilson et al., 1998) and SCORE function (Conroy et al., 2003) were used to estimate the 10 year cardiovascular risk. These are mathematical probability models generated using multivariate analysis. Framingham risk equation (Wilson et al., 1998) evaluates the chances of developing any fatal and non fatal cardiovascular events like angina, myocardial infarction, stroke, other type of coronary ischemia, congestive heart failure, intermittent claudication or peripheral arterial ischemia. The Framingham score is generated using the variables of age, gender, total cholesterol, high density lipoprotein (HDL) cholesterol, systolic arterial pressure, diabetes mellitus and smoking habit. CHD risk is estimated in terms of percentage and is categorized arbitrarily into as low risk (<10%) and high risk (>10%). The SCORE function (Conroy et al., 2003) estimates the risk for CMR within next 10 years. It predicts the cardiovascular mortality which may be attributed to coronary disease, sudden cardiac death, stroke, aortic aneurism, and heart failure. The SCORE function is based on the age, gender, total cholesterol, HDL cholesterol, systolic arterial pressure, and smoking status. Framingham risk score and SCORE function can be calculated by using various websites [Framingham risk equation – (<http://www.framinghamheartstudy.org/risk/coronary.html>) and SCORE function at website (<https://escol.escardio.org/heartscore/calc.aspx?model=europehigh>)]. Patients can be classified according to the probability of presenting “very high/high” CHD risk if they have Framingham function of $\geq 10\%$ (Elmslie et al., 2009) and as having “high” CMR if they have SCORE function of $\geq 5\%$ (Elmslie et al., 2009; Hartz et al., 2005). For patients with diabetes mellitus, the SCORE function may be multiplied by two for men and four for women to estimate the risk for cardiovascular mortality (Van Winkel et al., 2008; Nagpal and Bhartia, 2008).

Body weight, height and waist circumference were measured using calibrated scales. A point midway between the inferior costal margin and the superior iliac crest at the end of normal expiration in standing position was used to estimate the waist circumference. Blood pressure was assessed in supine position by using the standard mercury manometer. At least two readings were taken five

minutes apart for the blood pressure and lower value was taken into consideration for assessment of MS. If any patient had systolic blood pressure of ≥ 130 or diastolic blood pressure of >90 , then a third reading was taken after 30 minutes and the lowest of all the three readings was considered. A venous blood sample was collected under aseptic conditions after overnight fasting to estimate blood sugar (FBS), total cholesterol, triglycerides (TGA) and HDL.

MS was defined by the consensus definition (Expert Panel on Detection and Treatment of High Blood Cholesterol in Adults, 2001; Alberti et al., 2006), according to which presence of any of three out of five risk factors is sufficient for the diagnosis of MS. The consensus definition also recommends the use of population and country-specific definitions for defining the waist circumference cutoff (Alberti et al., 2006).

Patients found to be at high risk for cardiovascular events and mortality and those with metabolic abnormalities were informed about the need for life style modifications including proper diet and regular exercise, and were referred to specialist care.

Statistical analysis was carried out by using the SPSS version 14.0 for Windows (Chicago, Illinois, USA). Nominal and ordinal variables were studied in terms of frequencies and percentages, whereas the continuous variables were studied by using the mean and standard deviation. Comparisons were done by using Chi-Square test and *t*-tests. For variables with skewed distribution, non-parametric tests were used for comparison.

3. Results

During the study period 105 inpatients were diagnosed to have bipolar disorder. Seven patients were admitted twice, but the data with respect to cardiovascular factors and MS at the first instance during the study period was included. Of the 98 patients, 93 patients were aged ≥ 20 years and these patients formed the study cohort. Five patients were not included because, three refused to participate and data was not complete for two patients.

Sociodemographic and clinical profile of the sample: as depicted in Table 1, mean age of the patients was 39.5 years, the mean number of years of formal education was 11 years and mean duration of illness was 7 years. Majority of the participants were male, married, from urban locality and Hindu by religion. Nearly half of patients were on paid employment and belonged to a nuclear family.

Most patients were diagnosed with bipolar disorder, current episode mania with or without psychotic symptoms (68.8%) followed by bipolar disorder, current episode of depression with or without psychotic symptoms (20.4%). A minority of the patients (12.9%) were receiving antidepressants. The most commonly prescribed antipsychotic was olanzapine followed by quetiapine. In terms of conventional mood stabilizers, a higher percentage of patients were on valproate. The most commonly prescribed benzodiazepine was clonazepam followed by lorazepam.

Cardiovascular risk factors: prevalence of various cardiovascular risk factors is shown in Table 2. Low HDL level was the most common cardiovascular risk factor seen in the study group, followed by higher age (≥ 40 M, ≥ 45 F), hyperglycemia, high diastolic pressure and high cholesterol level. There were very few patients with high systolic blood pressure, diabetes mellitus and there were very few patients who were smoking tobacco.

Framingham function/risk equation score for the study sample was 3.36%. SCORE value was 1.73 and only 10.7% of the sample was found to have very high/high CHD risk (≥ 10) and 6.45% of the sample had high CMR risk (≥ 5).

Compared to females, a significantly higher proportion of males were older (≥ 40 M, ≥ 45 F) (56.1% vs 33.3%; χ^2 3.95*, $p < 0.05$), were smoking tobacco (18.1% vs 0; χ^2 5.36*, $p < 0.05$), had higher Framingham score (4.09 ± 5.75 vs 1.59 ± 1.05 , *U* value – 634.5*,

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