# Original Article

# A Cross-sectional Study to Estimate Cardiovascular Risk Factors in Patients with Bipolar Disorder

**Swetha Reddy Damegunta, Prasad Rao Gundugurti**

ABSTRACT

**Background:** There is increasing recognition of cardiovascular mortality and comorbidity in bipolar disorder (BD) in the recent times. Framingham 10 years risk of coronary heart disease (CHD) has been a widely accepted as a reliable estimate of cardiovascular risk in the general population. A few studies have estimated the relative risk of developing CHD in BDs, in India. We attempt to present a cross-sectional data from a prospective study to estimate the 10 years cardiovascular risk in BD population. **Subjects and Methods:** A total of 50 patients with BD aged between 20 and 60 years fulfilling the inclusion and exclusion criteria were enrolled into this study. Demographic variables and clinical evaluations including smoking history, medical and pharmacologic treatment history, physical examination, anthropometric measurements, and clinical laboratories for metabolic profiles were assessed. Using the Framingham 10-year risk questionnaire, the risk for each patient was calculated and compared with that of normal healthy control group. **Results:** The risk of developing a future cardiovascular event was 3.26% in BD and 2.02% in controls. We identified that a higher age at onset of illness, waist-hip ratio, total cholesterol, and unemployment showed a strong positive correlation with future CHD risk whereas administration of valproate, lithium for management of BD, higher socioeconomic status and educational status, and nonsmokers was associated negatively with the future CHD risk. **Conclusions:** It appears that there is a significant association between BD and metabolic factors, CHD, sociodemographic variables, and underscores the predictive ability of Framingham risk score in detecting cardiovascular diseases.

**Key words:** *Bipolar disorder, Framingham cardiovascular risk, metabolic syndrome*

## INTRODUCTION

In recent years, there has been increasing recognition of the influence of mental health on cardiovascular diseases (CVD) and their risk factors[1] causing premature mortality and morbidity. The mean 10-year risk for CVD and its outcomes (estimated according to both British and Framingham definitions) were consistently higher in participants with psychiatric disorders compared with controls, a high proportion of people whose level of cardiovascular risk exceeds the threshold for intervention are not receiving appropriate treatment.[2]

In bipolar disorders (BDs), the most frequent cause of death is with CVD.[3] Cardiovascular risk factors such

| Access this article online | |
|---|---|
| **Website:** www.ijpm.info | Quick Response Code |
| **DOI:** 10.4103/IJPSYM.IJPSYM_369_17 | |



**How to cite this article:** Damegunta SR, Gundugurti PR. A cross-sectional study to estimate cardiovascular risk factors in patients with bipolar disorder. Indian J Psychol Med 2017;39:634-40.

Asha Bipolar Clinic, Asha Hospital, Hyderabad, Telangana, India

**Address for correspondence:** Dr. Swetha Reddy Damegunta
F-16/A, Madhura Nagar, Behind Ratnadeep Supert Mart, Yousufguda, Hyderabad - 500 038, Telangana, India. E-mail: dr.sweetha@gmail.com

as obesity, metabolic syndrome, and diabetes mellitus type II (DM II) disorder are underrecognized and sub optimally treated and these risk factors independently exert deleterious effects on its course.[4]

Hypertension, hyperlipidemia, smoking, obesity, DM-II, and physical inactivity had been identified as potential CVD risk factors by Framingham Heart Study (FHS) (1948). The Framingham cardiovascular risk score Framingham risk score (FRS) developed from the FHS is one of a number of scoring systems used to determine an individual's chances of developing CVD in future, and it is validated across many populations. It reliably and accurately predicts CVD risk.[5,6] These scoring systems not only estimate the probability of a person who may develop CVD within the next 5 or 10 years but also indicates who is most likely to benefit from prevention and intervention.[7]

An individual's risk for future cardiovascular events is modifiable. Hence, early identification of the risk factors in individuals and taking appropriate preventive measures in patients with severe mental disorders, especially in BD is an interesting challenge. This study explores the association between FRS and BDs, which offer the opportunity for early interventions to mitigate the risk against future cardiovascular outcomes in highly vulnerable population.

There is no published literature which studied the future CVD risk in BD predicted by FRS in southern India. To the best of our knowledge, this would be the first study in South India.

### Cardiovascular risk in South Asians

CVD has become a major clinical and public health problem. South Asian countries, namely India, Pakistan, Sri Lanka, Bangladesh, and Nepal representing a quarter of the world's population contribute to the highest proportion of CVD burden when compared with any other regions globally. This population carries the increased risk even if they migrate to other countries and have increased mortality due to CVD at a younger age in comparison to the local population.[8] Thus, there is a growing need for greater awareness and control of risk factors associated with CVD in these countries as argued by Mohan *et al*.[9]

## SUBJECTS AND METHODS

Fifty consecutive consenting adult men and women previously diagnosed with BD attending our hospital in Hyderabad, India for at least a year were recruited for this study between January of 2012 and April of 2013. Age- and sex-matched healthy controls with no past, present, and family histories of psychiatric illnesses were recruited from a general hospital setting during the same time. The subjects entered into this study were between the ages of 20–60 years. We excluded patients with any other psychiatric comorbidity. Subjects with any severe renal, hepatic dysfunction or any other severe medical disorder and pregnancy were excluded as they alter the blood pressure and serum lipid levels. However, people whose hypertension controlled with anti-hypertensive's and hypercholesterolemia controlled with lipid lowering agents were included.

### Case records

Sociodemographics, education and occupational status, and socioeconomic status (SES),[10] history of cigarette smoking, nicotine dependence assessed with Fagerstrom smoking questionnaire (FSQ),[11] duration and treatment of the psychiatric illness (recorded for the psychiatric cohort), history pertaining to DM-II and essential hypertension, including family history and the current status of treatment was recorded for all subjects. Relevant medical and psychiatric information was obtained from personal interviews and medical records. Anthropometric measures such as height, weight, waist, and hip circumference were recorded using standardized procedures. Body mass index (BMI) and waist-hip ratio (WHR) were also calculated for each subject. Blood pressure was recorded with sphygmomanometer in the right upper limb in sitting position. The study was approved by the Institutional Ethics Committee. Informed consent was obtained from the subjects before enrollment in the study.

#### *Laboratory assays*

A single venous blood sample was collected in evacuated tubes after an overnight fast of 12-14 h and analyzed for total cholesterol (TC) and high-density lipoprotein (HDL). The assays were performed in an accredited laboratory.

#### *Cardiovascular diseases risk assessment*

The cardiovascular risk for each subject was calculated using the Framingham 10 years risk calculator available on the webpage http://hp2010.nhlbihin.net/atpiii/calculator.asp.[12] Computed percentage risk estimates for the number of outcomes over the 10 years period was taken. This 10 years risk calculator is best suited for individuals free of coronary heart disease (CHD). Estimation of the risk differs for men and women. The risk factors such as age, TC, HDL, systolic blood pressure (SBP), treatment for hypertension, and smoking status are considered to arrive at a score, which calculates the hard CHD outcomes such as myocardial infarction, coronary insufficiency, angina pectoris, and coronary death. Each factor has been given a point (http://www.framinghamheartstudy.org/risk/hrdcoronary.html) and the FRS is arrived by addition

of the points according to the subjects' age, levels of TC and HDL, SBP, treatment for hypertension, and smoking status. The point total is then correlated with the 10 years risk[13] (http://www.framinghamheartstudy.org/risk/hrdcoronary.html).

### Statistical analyses

The demographics, illness, and other continuous variables were expressed as means ± standard deviations, and categorical variables (example: Men, women) as frequencies, and displayed them in tables for both the groups (i.e., persons with BD and healthy controls). Tests of proportion were carried out to investigate the interrelationship among the two groups of subjects after adjustment for gender and age. We considered $P < 0.05$ as statistically significant. Further, we employed multiple linear regression analysis to analyze the relationship between various independent variables and one dependent variable, i.e., the FRS for each subject.

## RESULTS

Characteristics of participants: Data pertaining to the two study cohorts were tabulated and analyzed at the end of the study period. Both the groups differed significantly in terms of secondary education, marital status, lower SES, [Table 1] FSQ, presence of DM-II, family history of DM-II, [Table 2] TC, and HDL [Table 3]. No significant difference was noted between the FRS of both the groups.

### Multiple linear regression analysis

#### *In bipolar disorder group*

Variables such as WHR, age at onset of illness, lower middle SES, TC levels, unemployment showed strong positive influence on the future CVD risk, whereas variables such as treatment with aripiprazole, risperidone, and quetiapine, duration of treatment, male gender, waist circumference (WC) and primary education showed weak positive influence on the CVD risk in future. Variables such as BMI, treatment with valproate, upper middle SES, single, nonsmokers, height showed strong negative influence on the future CVD risk whereas HDL cholesterol, higher education, treatment with lithium, and family history of medical illnesses were found have a weak negative influence on the future CVD risk [Table 4]. None of the variables is found to be independently associated with the increase in the FRS (variable inflation factor [VIF] = 2.6, $R^2$ – 0.9396 [Table 5]).

#### *In control group*

Variables such as age, male gender, BMI showed a strong positive influence and nonsmokers showed a strong negative influence on the future CVD risk [Table 6]. None of the variables is found to be independently associated with the increase in the FRS (VIF = 2.1, $R^2$ – 0.9592 [Table 7]).

**Table 1: Sociodemographic variables of participants in the study**

| | Subjects with bipolar disorder (*n*=50) | Controls (*n*=50) | *P* (*Z*) |
|---|---|---|---|
| Age, years (mean±SD) | 39.68±12.087 | 40.38±10.99 | 0.76 |
| Gender, *n* (%) | | | |
| Male | 34 (68) | 25 (50) | 0.07* (−1.830) |
| Female | 16 (32) | 25 (50) | 0.07* (1.830) |
| Education, *n* (%) | | | |
| Primary | 3 (6) | 8 (16) | 0.12 (1.598) |
| Secondary | 25 (50) | 15 (30) | 0.05** (−2.041) |
| Graduation | 22 (44) | 24 (48) | 0.68 (0.401) |
| Postgraduation | 0 | 3 (6) | 0.6 (0.549) |
| Employment, *n* (%) | | | |
| Unemployed | 28 (56) | 19 (38) | 0.08* (−1.803) |
| Employed | 22 (44) | 31 (62) | 0.08* (1.803) |
| Marital status, *n* (%) | | | |
| Married | 41 (82) | 48 (96) | 0.03** (2.237) |
| Single | 9 (18) | 2 (4) | 0.03** (−2.237) |
| SES, *n* (%) | | | |
| Upper | 1 (2) | 3 (6) | 0.31 (1.021) |
| Upper middle | 11 (22) | 13 (26) | 0.64 (0.468) |
| Middle | 32 (64) | 29 (58) | 0.54 (−0.615) |
| Lower middle | 6 (12) | 0 | 0.02** (2.526) |
| Lower | 0 | 5 (10) | 0.02** (2.294) |

*Proportions significantly different at 90% ($P<0.1$); **Proportions significantly different at 95% ($P<0.05$); ***Proportions significantly different at 99% ($P<0.01$). SD – Standard deviation; SES – Socioeconomic status

## DISCUSSION

The World Health Organization has projected that CVD will become the number one cause of morbidity and mortality in the world by the year 2015,[14] and it is expected that Indians would be the most affected among all ethnic populations.[15] Atherosclerotic CVD represented 30% of all global deaths (17.5 million deaths) in 2005,[16] 2.3 million deaths reported only in India in the year 1990; this is projected to double by the year 2020.[17] Forouhi *et al.* found that CHD mortality was 50% higher in people born in Indian subcontinent than among people born in England.[18]

Several studies have found mortality rates between 1.5 and 2.5 times higher in BD patients than the general population.[19,20] Kilbourne *et al*.[21] stated that alternating manic and depressive episodes in BD attributed to an increased "allostatic load," defined as the "wear-and-tear" on the body and brain.

### Global burden

The global burden caused by these illnesses showed that disability adjusted life-years (in millions) for BD

**Table 2: Clinical characteristics of participants in the study**

| | Subjects with bipolar disorder (*n*=50) | Controls (*n*=50) | *P* (*Z*) |
|---|---|---|---|
| Smoking status, *n* (%) | | | |
| Nonsmoker | 38 (76) | 40 (80) | 0.63 (0.483) |
| Smoker | 12 (24) | 10 (20) | 0.63 (−0.483) |
| FSQ (mean±SD) | 4.33±0.65 | 3.1±1 | 0.008*** |
| Duration of illness in years (mean±SD) | 9.58±4.86 | | |
| Duration of treatment in year (mean±SD) | 5.89±4.86 | | |
| Distribution of pharamcotherapeutic agents (%) | | | |
| Quetiapine | 8 | | |
| Aripiprazole | 2 | | |
| Risperidone | 18 | | |
| Lithium | 13 | | |
| Valproate | 30 | | |
| History of, *n* (%) | | | |
| Diabetes type II | 1 (2) | 7 (14) | 0.03** (2.212) |
| Hypertension | 12 (24) | 5 (10) | 0.07* (−1.864) |
| Both | 4 (8) | 1 (2) | 0.17 (−1.376) |
| Treated for medical illness, *n* (%) | | | |
| Yes | 16 (32) | 11 (22) | 0.27 (−1.126) |
| No | 34 (68) | 39 (78) | 0.27 (1.126) |
| Family history of medical illness, *n* (%) | | | |
| Diabetes type II | 2 (4) | 10 (20) | 0.02** (2.462) |
| Hypertension | 9 (18) | 6 (12) | 0.41 (0.840) |
| Both | 4 (8) | 7 (14) | 0.35 (0.959) |

*Proportions significantly different at 90% ($P<0.1$), **Proportions significantly different at 95% ($P<0.05$), ***Proportions significantly different at 99% ($P<0.01$). FSQ – Fagerstrom smoking questionnaire; SD – Standard deviation

**Table 3: Metabolic parameters of participants in the study**

| | Subjects with bipolar disorder (*n*=50) | Controls (*n*=50) | *P* |
|---|---|---|---|
| Height (mean±SD) | 1.6512±0.78 | 1.6362±0.77 | 0.93 |
| Weight (mean±SD) | 73.28±10.5 | 69.34±11.71 | 0.08* |
| BMI (mean±SD) | 26.87±3.6 | 25.96±3.98 | 0.23 |
| WC (mean±SD) | 91.06±16.04 | 84.41±21.68 | 0.08* |
| WHR (mean±SD) | 0.92±0.06 | 0.91±0.09 | 0.51 |
| SBP (mean±SD) | 122.40±8.22 | 122.60±9.22 | 0.09 |
| TC (mean±SD) | 172.16±28.72 | 158.02±15.51 | 0.003*** |
| HDL (mean±SD) | 34.7±7.1 | 46.68±3.01 | 0.00*** |
| FRS in next 10 years (mean±SD) | 3.26±6.4 | 2.02±6.7 | 0.07* |

*Proportions significantly different at 90% ($P<0.1$); **Proportions significantly different at 95% ($P<0.05$); ***Proportions significantly different at 99% ($P<0.01$). BMI – Body mass index; WC – Waist circumference; WHR – Waist hip ratio; SBP – Systolic blood pressure; TC – Total cholesterol; HDL – High-density lipoprotein; FRS – Framingham risk score; SD – Standard deviation

is 12.9 in middle- and low-income countries[22] and is projected to rise to 14.7% by 2020. Although neurologic and psychiatric disorders comprise only 1.4% of all deaths, they account for a remarkable 28% of all years of life lived with a disability.[23]

## Cardiovascular risk factors in bipolar disorder

### *Cardiovascular diseases risk score*

The future CVD risk (3.2) was low in our study population compared with those reported by Correll *et al*. 2008 (4.7),[24] Garcia-Portilla *et al*. 2009 (7.75),[19] Montes *et al*. 2009 (7.3).[25] Other studies showed that 19% of their study population had CVD risk >10,[26] <20.[27] This could be explained on the basis that our sample size was small and prevalence of CVD risk factors was low when compared to those studies.

### Age

Compared to other studies[19,25,28] which reported high CVD risk, we had a younger study population ($\mu = 39.68$, $\sigma = 12.08$). We found a 4-fold increase in CVD risk with a year increase in age of our study group.

### Social gradient

The evidence for greater risk of CVD in low-socioeconomic strata has been well established and reinforced with the findings in our study. The urban–rural differences in India has a pronounced effect on the outcome

**Table 4: Estimates for various independent variables of patients with bipolar disorder**

| Independent variables | Estimates (SD beta)* | Predictability power | VIF** |
|---|---|---|---|
| WHR | 12.78842694 | Strong predictive | 2.505 |
| Age | 4.13071883 | Strong predictive | 3.808 |
| Lower middle SES | 1.083697931 | Strong predictive | 1.377 |
| Unemployed | 0.42753268 | Strong predictive | 2.386 |
| TC | 0.06441489 | Strong predictive | 2.568 |
| BMI | 0.091100879 | Strong predictive | 4.949 |
| Valproate | −0.880888659 | Strong predictive | 3.049 |
| Upper middle SES | −0.966857529 | Strong predictive | 2.22 |
| Single | −1.823337244 | Strong predictive | 2.911 |
| Nonsmoker | −6.197170277 | Strong predictive | 2.471 |
| Height | −10.09493384 | Strong predictive | 3.46 |
| Resperidone | 0.912742505 | Medium predictive | 1.667 |
| WC | 0.015771078 | Medium predictive | 3.578 |
| Family history of medical illness | −0.092040747 | Medium predictive | 2.278 |
| HDL | −0.115748086 | Medium predictive | 1.924 |
| Lithium | −1.736384351 | Medium predictive | 2.218 |
| Noncompliance | 0.354066133 | Weak predictive | 1.901 |
| Medical history | 0.326686879 | Weak predictive | 4.478 |
| SBP | 0.159858893 | Weak predictive | 3.27 |
| Graduation | −0.334733242 | Weak predictive | 2.32 |
| Aripiprazole | 2.794222941 | Weak predictive | 1.374 |
| Male | 2.081743739 | Weak predictive | 3.862 |
| Treatment duration for BD | 1.761158595 | Weak predictive | 1.448 |
| Quetiapine | 1.313577575 | Weak predictive | 2.615 |
| Primary education | 1.23280731 | Weak predictive | 1.914 |

*No sign indicates that independent variable is directly proportional to the CVD risk and "-" sign indicates that independent variable is indirectly proportional to the CVD risk, **The amount of inflation created by all other independent variables. CVD – Cardiovascular disease; SES – Socioeconomic status; VIF – Variable inflation factor; BMI – Body mass index; HDL – High-density lipoprotein; SBP – Systolic blood pressure; BD – Bipolar disorders; WC – Waist circumference; WHR – Waist hip ratio; TC – Total cholesterol

**Table 5: The efficiency of the above model [i.e., Table 4]***

| | |
|---|---|
| $R^2$* | 0.9396 |
| Adjusted $R^2$ | 0.8767 |

*Percentage of variance explained by all the independent variables. This indicates the efficiency of the model. It lies between 0 and 1. The higher the $R^2$, the better the model

of CVD and is often cumulative, resulted in higher mortality rates among the poor when compared to the rich, adjustments for which eliminated the mortality difference among the two groups.[29]

### Education

We could establish the findings of other such similar studies[29,30] in which, the primary level of education was associated with an increased risk of future CVD. We also found that higher the level of education, the risk of future CVD decreased.

### Tobacco use

Our study has shown that there is decreased CVD risk associated with nonsmokers. An Australian study established an increased cardiovascular risk in people with mental illness who were either smokers or ex-smokers compared to that of controls.[26] A study reported that 44% with BD were current smokers.[27]

### History of medical illnesses

The prevalence of medical illness in patient and their family members is low in our study. The presence of medical illnesses such as DM-II and hypertension increases the CVD risk.[19]

### Anthropometric measures

Our study found a strong positive correlation with WHR and future CVD risk. Truncal obesity WC is significantly associated with increased risk of future CVD.[28,31] This area leaves a lot of scope for further research as it was not been studied so far in BD.

### Total cholesterol and high density lipoprotein cholesterol

In this study, TC had shown to increase the future CVD risk minimally whereas the risk decreases with increase in HDL cholesterol. A large study of ten industrial populations has highlighted that dyslipidemia is higher among the more educated and people with mental illness, irrespective of diagnosis, had higher prevalence of metabolic syndrome, especially dyslipidemia and disorders of glucose homeostasis.[29]

### Effect of psychotropics on cardiovascular diseases

Surprisingly, aripiprazole, quetiapine, and risperidone and the duration of treatment was associated with higher risk

**Table 6: Estimates for various independent variables of controls**

| Independent variables | Estimates (SD beta) | Predictive power | VIF |
|---|---|---|---|
| Age | 5.095745329 | Strong predictive | 1.877 |
| Male | 3.284162803 | Strong predictive | 3.087 |
| BMI | 0.218294487 | Strong predictive | 2.292 |
| Nonsmoker | −7.548121097 | Strong predictive | 1.950 |
| Height | 0.701889233 | Medium predictive | 1.575 |
| SBP | 0.064699487 | Medium predictive | 1.95 |
| TC | 0.062276755 | Medium predictive | 1.499 |
| HDL cholesterol | −0.193249032 | Medium predictive | 1.899 |
| Primary education | −1.943338033 | Medium predictive | 2.577 |
| Treatment for medical illness | 1.306567747 | Weak predictive | 1.803 |
| Family history of medical illness | 0.367936334 | Weak predictive | 2.065 |
| Graduation | 0.364699756 | Weak predictive | 3.459 |
| WC | −0.020802414 | Weak predictive | 2.42 |
| Employment | −0.058564351 | Weak predictive | 3.903 |
| Middle SES | −0.53542091 | Weak predictive | 1.731 |
| Postgraduation | −0.715939425 | Weak predictive | 1.784 |
| Single | −1.13104264 | Weak predictive | 1.281 |
| Low SES | −1.168988801 | Weak predictive | 2.105 |
| WHR | −5.596806894 | Weak predictive | 2.529 |

VIF – Variable inflation factor; HDL – High-density lipoprotein; SES – Socioeconomic status; SD – Standard deviation; BMI – Body mass index; WC – Waist circumference; WHR – Waist hip ratio; SBP – Systolic blood pressure; TC – Total cholesterol

**Table 7: Efficiency of the above model [i.e., Table 6]**

| | |
|---|---|
| $R^2$* | 0.9592 |
| Adjusted $R^2$ | 0.9334 |

of future CVD. Whereas lithium and valproate decrease the future CVD risk. Pharmacological treatment with antipsychotics and mood stabilizers are the cornerstone of treatment for BD. Moreover, atypical antipsychotics are on the rise in prescriptions for BD in the recent times. However, they have adverse effects on lipid and glucose metabolism, predisposing patients to metabolic syndrome and therefore cardiovascular morbidity.[32]

## CONCLUSIONS

In summary, and based on our study, it appears that there is a significant association between BD and metabolic factors, CVD, sociodemographic variables, and underscores the predictive ability of FRS in detecting CVD.

In our study, the risk of developing a future cardiovascular event was 3.26% in BD and 2.02% in controls. We identified that a higher age at onset of illness, WHR, TC, and unemployment showed a strong positive correlation with future CVD risk, whereas administration of valproate, lithium for the management of borderline personality disorder, higher SES, and higher educational status, nonsmokers were associated negatively with the future CVD risk.

### Strengths of our study

Our findings confirm the results of several other studies and offer further insights into the nature of metabolic disease and CVD risk in BD.

Our study is designed to gather data on cardiovascular risk in a typical clinical setting. Ours is the first study of its kind in South India to estimate the 10 years cardiovascular risk by Framingham cardiovascular risk calculator and comparing with normal healthy controls.

### Limitations of our study

A major limitation of Framingham 10 years cardiovascular risk calculator is that it estimates the risk of developing CHD within only a 10 years period. Among young individuals, there is marked disparity between 10 years risk and lifetime risk in the FHS.

The results of our cross-sectional study do not predict the adverse cardiovascular risk for each group after 10 years because of the interim analysis at the end of 2 years. However, we are continuing to study the prospective data and analyze the long-term results and ascertain the usefulness of the Framingham risk calculator in estimating the future cardiovascular risk as well as the impact of prevention strategies in reducing the risk outcome.

### Implications of our study

On observations made from this study, improving physical health, educational levels, and preventing obesity, use antipsychotic medications with caution in patients with BD can decrease the risk of future CVD. Intervention can be aimed at bringing changes in the sedentary life style, dietary life style, smoking habits, psychosocial stressors, watch on weight gain and most importantly, the accessibility to the medical facilities.

The role of specific psychiatric diagnosis in increasing the risk of CVD has not been fully explored. Aggressive interventions to correct or improve the metabolic parameters associated with metabolic syndrome and CVD in BD is necessary, ideally within first 10 years of detection. Hence, there is a significant unmet need for identifying the risk factors, which would predict future cardiovascular events in the psychiatric patient population.

### Acknowledgments

We would like to thank all the participants in our study and Mr. Venugopal Kodumagulla for his statistical assistance.

**Financial support and sponsorship**
Nil.

**Conflicts of interest**
There are no conflicts of interest.

## REFERENCES

1. Gupta R, Joshi P, Mohan V, Reddy KS, Yusuf S. Epidemiology and causation of coronary heart disease and stroke in India. Heart 2008;94:16-26.
2. Jin H, Folsom D, Sasaki A, Mudaliar S, Henry R, Torres M, *et al.* Increased Framingham 10-year risk of coronary heart disease in middle-aged and older patients with psychotic symptoms. Schizophr Res 2011;125:295-9.
3. Osby U, Brandt L, Correia N, Ekbom A, Sparén P. Excess mortality in bipolar and unipolar disorder in Sweden. Arch Gen Psychiatry 2001;58:844-50.
4. McIntyre RS, Soczynska JK, Beyer JL, Woldeyohannes HO, Law CW, Miranda A, *et al.* Medical comorbidity in bipolar disorder: Re-prioritizing unmet needs. Curr Opin Psychiatry 2007;20:406-16.
5. Marrugat J, Subirana I, Comín E, Cabezas C, Vila J, Elosua R, *et al.* Validity of an adaptation of the Framingham cardiovascular risk function: The VERIFICA Study. J Epidemiol Community Health 2007;61:40-7.
6. Lloyd-Jones DM, Wilson PW, Larson MG, Beiser A, Leip EP, D'Agostino RB, *et al.* Framingham risk score and prediction of lifetime risk for coronary heart disease. Am J Cardiol 2004;94:20-4.
7. Willis A, Davies M, Yates T, Khunti K. Primary prevention of cardiovascular disease using validated risk scores: A systematic review. J R Soc Med 2012;105:348-56.
8. Ramaraj R, Chellappa P. Cardiovascular risk in South Asians. Postgrad Med J 2008;84:518-23.
9. Mohan V, Deepa M, Farooq S, Prabhakaran D, Reddy KS. Surveillance for risk factors of cardiovascular disease among an industrial population in southern India. Natl Med J India 2008;21:8-13.
10. Tiwari SC, Kumar A, Kumar A. Development & standardization of a scale to measure socio-economic status in urban & rural communities in India. Indian J Med Res 2005;122:309-14.
11. Fagerstrom KO, Heatherton TF, Kozlowski LT. Nicotine addiction and its assessment. Ear Nose Throat J 1990;69:763-5.
12. National Heart Lung and Blood Institute (internet). (Place unknown): Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III); 2002. Available from: http://www.hp2010.nhlbihin.net/atpiii/calculator.asp. [Last updated on 2004 Apr].
13. Wolf PA. Framigham Heart Study (internet). Boston: Framinghan Heart Study; 2013. Available from: http://www.framinghamheartstudy.org/risk/hrdcoronary.html. [Last updated on 2013 Jun 07].
14. Fuster V, Kelly BB. Promoting Cardiovascular Health in the Developing World. A Critical Challenge to Achieve Global Health. Washington, DC: The National Academic Press; 2010.
15. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. Lancet 1997;349:1498-504.
16. World Health Organization. World Health Statistics Annual 2005. Geneva: World Health Organization; 2005. Available from: http://www.who.int/en/. [Last accessed on 2007 Aug 10].
17. Gupta R. Trends in hypertension epidemiology in India. J Hum Hypertens 2004;18:73-8.
18. Forouhi NG, Sattar N, Tillin T, McKeigue PM, Chaturvedi N. Do known risk factors explain the higher coronary heart disease mortality in South Asian compared with European men? Prospective follow-up of the Southall and Brent studies, UK. Diabetologia 2006;49:2580-8.
19. Garcia-Portilla MP, Saiz PA, Bascaran MT, Martínez AS, Benabarre A, Sierra P, *et al.* Cardiovascular risk in patients with bipolar disorder. J Affect Disord 2009;115:302-8.
20. Roshanaei-Moghaddam B, Katon W. Premature mortality from general medical illnesses among persons with bipolar disorder: A review. Psychiatr Serv 2009;60:147-56.
21. Kilbourne AM, Brar JS, Drayer RA, Xu X, Post EP. Cardiovascular disease and metabolic risk factors in male patients with schizophrenia, schizoaffective disorder, and bipolar disorder. Psychosom Med 2007;48:412-7.
22. Collins PY, Patel V, Joestl SS, March D, Insel TR, Daar AS; Scientific Advisory Board and the Executive Committee of the Grand Challenges on Global Mental Health, *et al.* Grand challenges in global mental health. Nature 2011;475:27-30.
23. Menken M, Munsat TL, Toole JF. The global burden of disease study: Implications for neurology. Arch Neurol 2000;57:418-20.
24. Correll CU, Frederickson AM, Kane JM, Manu P. Equally increased risk for metabolic syndrome in patients with bipolar disorder and schizophrenia treated with second-generation antipsychotics. Bipolar Disord 2008;10:788-97.
25. Montes JM, Vieta E, González-Pinto A, Rejas-Gutiérrez J, Mesa F. PW05-02 Cardiovascular Risk in a Spanish Population of Bipolar Disorder Patients: Results from the BIMET Study. Vol. 24. European Psychiatry 17th EPA Congress – Lisbon, Portugal, January, 2009. 2009. p. S360. [Abstract book].
26. Davidson M. Risk of cardiovascular disease and sudden death in schizophrenia. J Clin Psychiatry 2002;63:5-11. Erratum appears in: J Clin Psychiatry 2002;63:744.
27. Dickerson F, Stallings CR, Origoni AE, Vaughan C, Khushalani S, Schroeder J, *et al.* Cigarette smoking among persons with schizophrenia or bipolar disorder in routine clinical settings, 1999-2011. Psychiatr Serv 2013;64:44-50.
28. Slomka JM, Piette JD, Post EP, Krein SL, Lai Z, Goodrich DE, *et al.* Mood disorder symptoms and elevated cardiovascular disease risk in patients with bipolar disorder. J Affect Disord 2012;138:405-8.
29. Narayanan G, Prabhakaran D. Integrating mental health into cardiovascular disease research in India. Natl Med J India 2012;25:274-80.
30. Gupta R, Gupta VP, Ahluwalia NS. Educational status, coronary heart disease, and coronary risk factor prevalence in a rural population of India. BMJ 1994;309:1332-6.
31. Wysokinski A, Kowman M, Kloszewska I. The prevalence of metabolic syndrome and Framingham cardiovascular risk scores in adult inpatients taking antipsychotics – A retrospective medical records review. Psychiatr Danub 2012;24:314-22.
32. Rahman FU, Rafiq A, Idrees M, Khan S, Parvez A. Lipid profile in schizophrenic patients on atypical antipsychotics. GJMS 2012;10:87-9.