



# Cardiovascular Comorbidity in Women with Bipolar Disorder

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## Learning Objectives

1. To study the cardiovascular diseases (CVD)/ CVD risk factors in women with BD .
2. To compare the CVD/CVD risk factors in women with BD to men with BD and women in general population.

## Background

Bipolar Disorder (BD) is a chronic psychiatric disorder with almost equal sex distribution for BD-I and female predominance for BD-II.<sup>1</sup> Patients with BD have a high medical comorbidity burden (30-60%). CVD have been reported as the most common medical comorbidity in BD with rates reaching 30%.<sup>2,3</sup> Despite well documented sex differences in CVD in general population, data on sex differences in BD patients with comorbid CVD is scarce. In this systematic review, we aimed to study the CVD comorbidity in women versus men in BD and in comparison, to women in general population.

## Methods

A comprehensive search of electronic databases including PubMed, PsycINFO, Embase, and SCOPUS was conducted. The eligibility criteria included Case-control/ Cohort/ Cross-sectional/ Retrospective/ Prospective/ Observational studies in English with gender data among BD patients. A total of 10 studies were identified in the literature that investigated the sex differences and the relationship between CVD/CVD risk factors and BD studies were included in this review

## Characteristics of studies on Cardiovascular Diseases in Women with BD

Reference	Study Description	Female bipolar N (%of BD)	Finding/result
Vance MC et al 2019	Design: Prospective cohort study , Veterans with mental illness Total sample: 1611 378 patients with mental illness Major outcome measures: 1. Cardiovascular disease ( CVD) event of combined CVD mortality+ first heart attack + first stroke, 2. CVD mortality Follow up duration: 5 years	11436(12.1)	<ul style="list-style-type: none"> <li>OR for 5 year CVD outcomes in women with BD for CVD event 1.36 (1.17-1.58) and CVD mortality 1.47 (1.17-1.85) ,p&lt;0.01 (Adjusted for psychiatric diagnosis, psychotropic medications, diabetes measures)</li> <li>Among women the associations between psychosis, BD, and depression and CVD events, and between psychosis and BD and CVD mortality, remained significant after adjusting for all psychiatric diagnosis.</li> </ul>
Martin DJ et al 2016	Design: Cross-sectional study Total Sample: 145 991 UK Biobank participants, Major outcome: Association between BD and cardiovascular, DM, HTN, Angina, MI and stroke. Sample was divided into 3 groups by a self-designed questionnaire for a lifetime history of clinical features of BD, Depression and controls	766(49.2)	<ul style="list-style-type: none"> <li>BD Women had higher OR for any cardiovascular disease (1.55, 95% CI 1.32–1.83 ) vs( 1.46, 95% CI 1.25–1.69 ) in BD men and for hypertension (1.46, 95% CI 1.24–1.73 ) in BD women v. (1.42, 95% CI 1.22–1.66) in BD men.</li> <li>Relative to controls, women with features of BD had a greater risk of 'any cardiovascular disease' than men with BD features (OR 1.36 v. 1.19)</li> </ul>
Wu Shu -I et al 2015	Design: Population cohort study, No. of BD patients : 12,119 BD, 58,106 SCZ, and 207,592 no serious mental illness, Major outcome: Development of Acute MI (AMI) Follow up duration : 11 years	6629(54.7)	<ul style="list-style-type: none"> <li>Hazard ratio for AMI for BD females was 1.87(1.46-2.4) vs BD males 1.38(1.1-1.74) (adjusted for age)</li> <li>Women with BD had a 1.5-fold higher adjusted risk of AMI than comparison groups.</li> <li>The cardio protective effect in younger women was apparently attenuated in the mental disorder group.</li> </ul>
Boden R et al 2014	Design: Population cohort study , No. of BD patients: 442 BD patients with MI Major outcome: Mortality after MI in patients with 442 BD and 541 SCZ and compared to 208609 controls without mental illness Follow up duration : 13 years	170(38.5)	<ul style="list-style-type: none"> <li>1 year mortality after first MI in BD female/control female = 1.19(0.72,1.97).</li> <li>1 year mortality after first MI in BD male/control male = 1.54(1.01,2.33).</li> <li>First MI occurred at an early age in patients with BD and SCZ as compared to controls.</li> </ul>
Westman J et al 2013	Design: Population based cohort study, Total sample: 17101 BD diagnosis with inpatient admissions Major outcome: Mortality rate ratios (MRR), excess mortality (excess deaths), cardiovascular disorder (CVD) assessed Follow up duration : 20 years	Unknown	<ul style="list-style-type: none"> <li>Men and women with BD were twice as likely to die of CVD compared to the general population (MRR 2.03; 95% CI1.93 to 2.13)</li> <li>Women with BD had higher MRR for somatic deaths and suicide and other external deaths as compared to BD males.</li> <li>BD Patients with deaths due to CVD were younger than people in the general population.</li> </ul>
Smith D.J et al 2013	Design: Population based cross-sectional study, No. of BD Patients: 2,582 BD patients Major outcome: multimorbidity and cardiovascular risk factors studied	1561(60.5)	<ul style="list-style-type: none"> <li>Women with BD were significantly more likely to have &gt;= 3 physical conditions than BD men (25.0% versus 17.0%; P &lt;0.001 ).</li> <li>BD patients vs controls had higher prevalence of CKD (7.3% vs 2.4%; OR 2.42 P &lt;0.001), thyroid disorders (16.6% vs 5.0%; OR 2.39 P &lt;0.001), chronic pain (17.5% vs 8.8%; OR 1.88 P &lt;0.001), COPD (6.6% vs 3.7%; OR 1.39 P &lt;0.001), and DM(8.4% vs 5.2%; OR 1.31 P &lt;0.001), but lower rates of HTN and atrial fibrillation.</li> </ul>
Garcia-Portilla M.P et al 2008	Design: Naturalistic multicenter cross-sectional stud Total Sample:194 BD patients (mean age 46.6yrs) Major outcome: cardiovascular risk factors and Systematic Coronary Risk Evaluation (SCORE) function for cardiovascular mortality risk (CMR) and the Framingham function to estimate the overall risk for CHD .	99(51.0)	<ul style="list-style-type: none"> <li>The overall risk of CHD was 7.6% (SD 7.4) and was significantly higher in BD males than in BD females (10.2% vs 4.7, p &lt;0.001),no gender differences in CMR though. Also there was a significantly greater proportion of BD males in the very high/high CHD (34.2% versus 11.6%, pb0.01) groups..</li> <li>In BD females, both CMR and CHD risk were significantly greater in those with metabolic syndrome (1.6 vs 0.5, p&lt;0.05 and 8.7 vs 3.3, p&lt;0.005, respectively).</li> <li>The risk of CHD and the CMR in ten years significantly increased with age in both BD males and BD females (p&lt;0.001), with the exception of females aged 65 or more.</li> </ul>
Lin H.C et al 2008	Design: Retrospective cohort study No of BD patients: 1429 BD patients; control: 4993 appendectomy patients Major outcome: risk of acute MI(AMI) in BD following acute mood episode, Follow up: 6 years	785(55)	<ul style="list-style-type: none"> <li>AMI occurred among 2.24% of BD Patients ( 2.29 females,2.17 in males )and 1.72% of controls(females 1.46,males 1.94).</li> <li>Male bipolar patients were more frequently overweight than females, but BD females had significantly higher rates of extreme obesity than males .</li> </ul>
Birkenaes A.B et al 2007	Design: Retrospective cohort study No of BD patients: 110; SCZ: 163 Major outcome: cardiovascular risk factors were compared between BD and SCZ Follow up duration: 3 years	67(60.9)	<ul style="list-style-type: none"> <li>Female BD had higher HDL-C (p&lt;0.01) and higher SBP (p&lt;0.05) as compared to SCZ female.</li> <li>Low HDL -C in SCZ and DM more in BD was statistically significant .</li> </ul>
Johannessen.L et al 2006	Design :Population Register cohort study No. of BD Patients: 25339 BD patients Major outcome: risk of HTN was studied	16450(64.9)	<ul style="list-style-type: none"> <li>Incidence rate ratio (IRR) in BD females 1.24(1.11-1.39) and BD males is 1.34(1.14-1.57)</li> <li>HTN was found in (2.46%) BD females, 2.20% in BD males, 2.17% in female controls.</li> </ul>

## Results

- Five large sample population studies have reported higher risk for CVD and mortality due to CVD in the BD group as compared to the general population.
- Women with BD were reported to be at higher risk of developing MI at early age, other CVD like hypertension, and higher mortality due to CV events as compared to the women in the general population.
- The risk of CV events and mortality was comparable among women and men with BD in majority of the studies.
- A small retrospective study underscored twice the prevalence of CVD risk factors in BD females in comparison to general population.
- A higher risk of MI at an early age for women with BD has been reported in comparison to women in general population.
- Also, a correlation among obesity, metabolic syndrome, and CVD has been underscored in women with BD.

## Conclusion

- In the BD population, the risk of CVD in women is comparable to men.
- The risk of CVD is much higher in BD women in comparison to women in general population.
- There is also a younger age of onset of CVD/MI in premenopausal women with BD in comparison to general population.
- The findings can be pointing at attenuated estrogen protective mechanism in women with BD, thus predisposing them to an early onset of CVD.

## References

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