# General medical comorbidities in Brazilian outpatients with bipolar disorder type I

## Comorbidades médicas em pacientes ambulatoriais com transtorno do humor bipolar tipo I

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## Abstract

**Background:** Bipolar disorder (BD) has been associated with high rates of general medical comorbidities (GMC) and medical risk factors. There have been scarce reports about this prevalence in Brazilian subjects with BD. **Objective:** Describe the prevalence of GMC in a sample of BD type I patients. **Methods:** Clinical records of 195 patients with BD type I were reviewed for identification of GMC. Patients with and without GMC were compared using the Mann-Whitney nonparametric test and the chi-Square test. **Results:** Sixty-three percent of patients had at least one medical comorbidity. The most prevalent conditions were: migraine (31.8%), hypothyroidism (24.1%), hypertension (11.3%), traumatic brain injuries (10.3%), asthma (9.7%), epilepsy (8.2%), diabetes (5.1%), stroke (2.1%) and hyperthyroidism (1%). Age and duration of illness were positively associated with the presence of GMC ($p < 0.001$). **Discussion:** In our study, in accordance with previous reports, the majority of patients presented at least one general medical disorder. The principal limitation of this study is the fact that diagnose of GMC was made based on self-report. There are scarce studies addressing GMC in the Brazilian population with BD and this report can contribute to improve diagnostic vigilance, assessment, treatment planning and decrease the burden associated with BD.

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**Keywords:** Bipolar disorder, general medical comorbidity, migraine.

## Resumo

**Contexto:** O transtorno do humor bipolar (THB) está associado a altas taxas de comorbidades médicas gerais (CMGs) e fatores de risco para problemas médicos, porém há escassos relatos sobre a prevalência dessas condições em brasileiros com THB. **Objetivo:** Descrever a prevalência de CMGs em uma amostra de pacientes com THB tipo I. **Métodos:** Dados clínicos de 195 pacientes com THB tipo I foram revisados para identificação de CMGs. Pacientes com e sem CMGs foram comparados usando o teste não paramétrico Mann-Whitney e o teste qui-quadrado. **Resultados:** Sessenta e três por cento dos pacientes relataram pelo menos uma comorbidade médica. As condições mais prevalentes foram: enxaqueca (31,8%), hipotireoidismo (24,1%), hipertensão (11,3%), traumatismo craniano (10,3%), asma (9,7%), epilepsia (8,2%), diabetes (5,1%), acidente vascular cerebral (2,1%) e hipertireoidismo (1%). Idade e duração da doença foram positivamente associadas à presença de CMGs ($p < 0,001$). **Conclusão:** Em concordância com relatos prévios, a maioria dos pacientes apresentou pelo menos uma doença médica. A principal limitação deste estudo reside no fato de o diagnóstico de CMGs ter sido baseado no autorrelato. Há escassos estudos visando à identificação de comorbidades médicas na população brasileira com THB e este estudo pode contribuir para melhor vigilância diagnóstica, avaliação, tratamento e diminuição da sobrecarga associada ao THB.

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**Palavras-chave:** Transtorno bipolar, comorbidades médicas, enxaqueca.

## Introduction

Bipolar disorder (BD) is a recurrent and chronic mental illness with lifetime prevalence rates estimated to be 3%-6% in the general population[1]. The disorder is characterized by mood episodes alternating with euthymic periods[2], and it is associated with functional decline[3,4], higher mortality rates and significant health care costs[3]. Comorbidities, high risk of suicide, social and professional impairment and low adherence to treatment increase the burden and cost of illness and worsen the prognosis[5].

Presence of one or more additional psychiatric disorders is the rule rather than the exception for BD. Data from the Stanley Foundation Bipolar Network indicate that 65% of patients with BD also have at least one comorbid lifetime axis I disorder and almost a quarter of these patients have three or more diagnoses[6]. In addition to their psychiatric illness, bipolar patients experience certain general medical comorbidities (GMC) at a higher rate than the general public. Compared with the general population, BD patients have a prevalence of diabetes mellitus approximately three times higher (9.9% *versus* 3.4%)[7], a prevalence of migraine more than two times higher (24.8% *versus* 10.3%)[8], and the mortality ratio of BD patients for cardiovascular disease is 3.0[1]. In the United States and Canada the lifetime prevalence of at least one medical disease varies from 7.2% to 64.3%[8-12].

Some of this excess morbidity has been associated with adverse effects of medications used to treat BD and also with lifestyle patterns, as is the case for obesity, diabetes, and hypothyroidism[7,13,14]. However, in most cases, the etiology of the comorbidity is not fully understood, as it is unclear whether a medical disorder is truly comorbid, is a consequence of treatment, or a combination of both[1,15].

Medical risk factors and GMC affect the course and the severity of BD as well as its treatment[2,16,17], and their impact is significant due to reasons including quality of life, delivery of psychiatry and medical services, mortality[10] and disability[18].

Individuals suffering from BD may be particularly at risk for obesity, a strong predictor of major medical problems including hypertension, cardiovascular disease, and diabetes mellitus, and

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the prevalence of this condition has been estimated between 8.3%-49%[13,16,17,19-23]. Obese bipolar patients experience a greater number of lifetime depressive and manic episodes, more severe and difficult-to-treat index affective episode[16], and are more likely to report a lifetime history of suicide attempts[17].

A cross-sectional study found that having a chronic medical disease was associated with less successful employment outcomes, greater dependency on others for assistance, more mental health hospitalizations, more mental health consultations, and more use of psychotropic medications in patients with BD[8]. Additionally, another research showed that GMC was associated with a worse quality of life especially in its physical domain[9].

Although several studies have shown a high prevalence of GMC in BD, there have been scarce reports about the prevalence of these conditions in Brazilian subjects with BD. The aim of the present study is to evaluate the prevalence of GMC in a sample of Brazilian outpatients with BD.

## Methods

The study was carried out at the Bipolar Disorder Research Program at the Institute of Psychiatry of the University of São Paulo Medical School. It was approved by the Institute's ethics committee and written informed consent was obtained from all subjects participating in the study. One hundred and ninety five outpatients with bipolar disorder type I (age ≥ 18 years old) were evaluated. All subjects were diagnosed according to the DSM-IV criteria using the Structured Clinical Interview for DSM-IV (SCID-P). Sociodemographic and clinical variables were reviewed and GMC was evaluated by a self-report questionnaire. This questionnaire assessed epilepsy, history of traumatic brain injuries, migraine, asthma, diabetes, hypothyroidism, hyperthyroidism, hypertension, and stroke and was administered during the patient's baseline evaluation. According to the answers the sample was divided in two groups: subjects who had at least one GMC and subjects who did not.

The statistical analysis was performed using the Statistical Package for the Social Sciences, version 14 (SPSS Inc., Chicago, IL, USA). The variables age; number of manic, depressive, mixed and total episodes; number of hospitalizations; number of suicide attempts and duration of illness were compared between the groups using Mann-Whitney nonparametric test. We also compared the variables gender, marital status and ethnicity using chi-square test. The level of statistical significance was set at alpha = 0.05.

## Results

The sociodemographic and clinical characteristics of the study sample are shown in table 1. Based on the overall sample the mean age was 39.2 years old (SD = 10.9), more than half were female (69.7%) and 42.6% were married. The largest ethnic group was Caucasian (75.4%), followed by Afro-American (22.5%), Asian (1.5%) and others (0.5%). The median number of total episodes was 7 (IR=9) and the mean duration of illness was 16.4 years (SD = 10.7). Nearly sixty-nine percent of the subjects had at least one GMC and the most prevalent conditions were: migraine (31.8%), hypothyroidism (24.1%), hypertension (11.3%), history of traumatic brain injuries (10.3%), asthma (9.7%), epilepsy (8.2%), diabetes (5.1%), stroke (2.1%), hyperthyroidism (1.0%) (Table 2). Twenty three percent of the sample had two or more GMC and 4.1% had 3 or more GMC. Age and duration of illness were positively associated with the presence of GMC ($p < 0.001$). No relationship was found between the presence of GMC and gender, marital status, ethnicity, number of episodes (manic, depressive, mixed and total), number of hospitalizations and number of suicide attempts. In order to correct for possible bias in the retrospective assessment of number of episodes, we divided the sample according to the median of total episodes and did not find any difference between the two groups on the presence of GMC.

**Table 1.** Clinical and demographic characteristics of the subjects

| Variables | |
|---|---|
| Age in years, mean (SD) | 39.2 (10.9) |
| Gender (female) | 69.7% |
| Marital status | |
| Married | 42.6% |
| Single | 39.5% |
| separated, divorced or widow | 17.9% |
| Ethnicity | |
| Caucasian | 75.4% |
| Afro-American | 22.5% |
| Asian | 1.5% |
| Other | 0.5% |
| Number of total episodes, median (IR)* | 7 (9) |
| Number of manic episodes, median (IR) | 3 (3) |
| Number of depressive episodes, median (IR) | 3 (5) |
| Number of mixed episodes, median (IR) | 0 (0) |
| Number of hospitalizations, median (IR) | 1 (2) |
| Number of suicide attempts, median (IR) | 0 (2) |
| Duration of illness in years, mean (SD) | 16.4 (10.7) |

* Underestimated number (some subjects reported a number of episodes as "too numerous to count").
IR: interquartile range.

**Table 2.** Prevalence of GMC in subjects with BD (n = 195)

| General medical comorbidity | N | % |
|---|---|---|
| Migraine | 62 | 31.8 |
| Hypothyroidism | 47 | 24.1 |
| Hypertension | 22 | 11.3 |
| History of traumatic brain injuries | 20 | 10.3 |
| Asthma | 19 | 9.7 |
| Epilepsy | 16 | 8.2 |
| Diabetes | 10 | 5.1 |
| Stroke | 4 | 2.1 |
| Hyperthyroidism | 2 | 1.0 |

## Discussion

Our findings are similar to prior studies in other populations pointing to an alarmingly higher prevalence of GMC among patients with BD when compared to the general population. In accordance with previous reports, the majority of subjects studied presented at least one concomitant medical disorder. The duration of illness was positively associated with the presence of GMC ($p < 0.001$) and it is in conformance with the findings of Soreca *et al.*[24], which described that medical burden was related to it.

Surprisingly, in our study, almost 32% of BD outpatients had migraine. We found in the literature a well-established association between migraine and depression, but among the BD population it has been indicated that BD II may co-exist with migraine more often than BD I[25-28]. It has been reported by other groups that these co-occurring diseases are associated with greater dysfunction, an increased risk of suicidal behaviour and comorbid anxiety disorders[8,25]. As migraine is associated with the female gender and we have a higher percentage of women in the sample, it is possible that migraine prevalence may be, in fact, an artifact of the unequal distribution of gender. Notwithstanding is known that bipolar women are more likely to suffer from migraine than men[8,29,30]. In addition, the use of a self-report instrument to determine the presence of migraine might overestimate the rate of migraine occurrence.

The second most prevalent condition was hypothyroidism (24.1%), and it may be related to the disease itself or to the medications used by these patients[31]. A recent study indicated that lithium, carbamazepine, and valproate might increase the risk of hypothyroidism, particularly if used together[14]. In our sample 72.3% of the patients had been using at least one of these three medications during the last year, which could potentially explain the high rate of this illness.

Excess cardiovascular mortality in BD has been documented for several years and hypertension, an important risk factor, is among the most common medical conditions and is a major contributor to increased treatment costs in BD[32-34]. In the present study, 11.3% of BD I subjects reported being diagnosed with arterial hypertension, although previous estimates for hypertension prevalence in BD patients were generally from 15 to 39%[17,33,35].

One of the limitations of the present study is that our results are based on an assessment by a self-report questionnaire of the patient's diagnosed GMC and in addition no standardized evaluation was applied to assess these illnesses.

Despite its limitations, there are scarce studies addressing GMC in the Brazilian population with BD and this report can contributes to improve diagnostic vigilance and helps clinicians tailor treatment strategies.

Our findings suggest the need for future studies addressing GMC and BD comorbidities and the necessity to optimize care and achieve the best possible treatment outcomes by integrating psychiatric and general medical care. Perhaps most importantly, preventive strategies are needed to reduce the excessive prevalence and impact of general medical disorder among people with BD.

In conclusion, Brazilian outpatients with BD type I have significant rates of GMC and medical risk factors. This report contributes to the knowledge in the field, and our findings support the need for future studies addressing these co-occurring diseases. Additionally, integrated care and the development of diverse therapeutic options, such as group therapy[36], diagnostic vigilance and comprehensive treatment are required and could be effective strategies.

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